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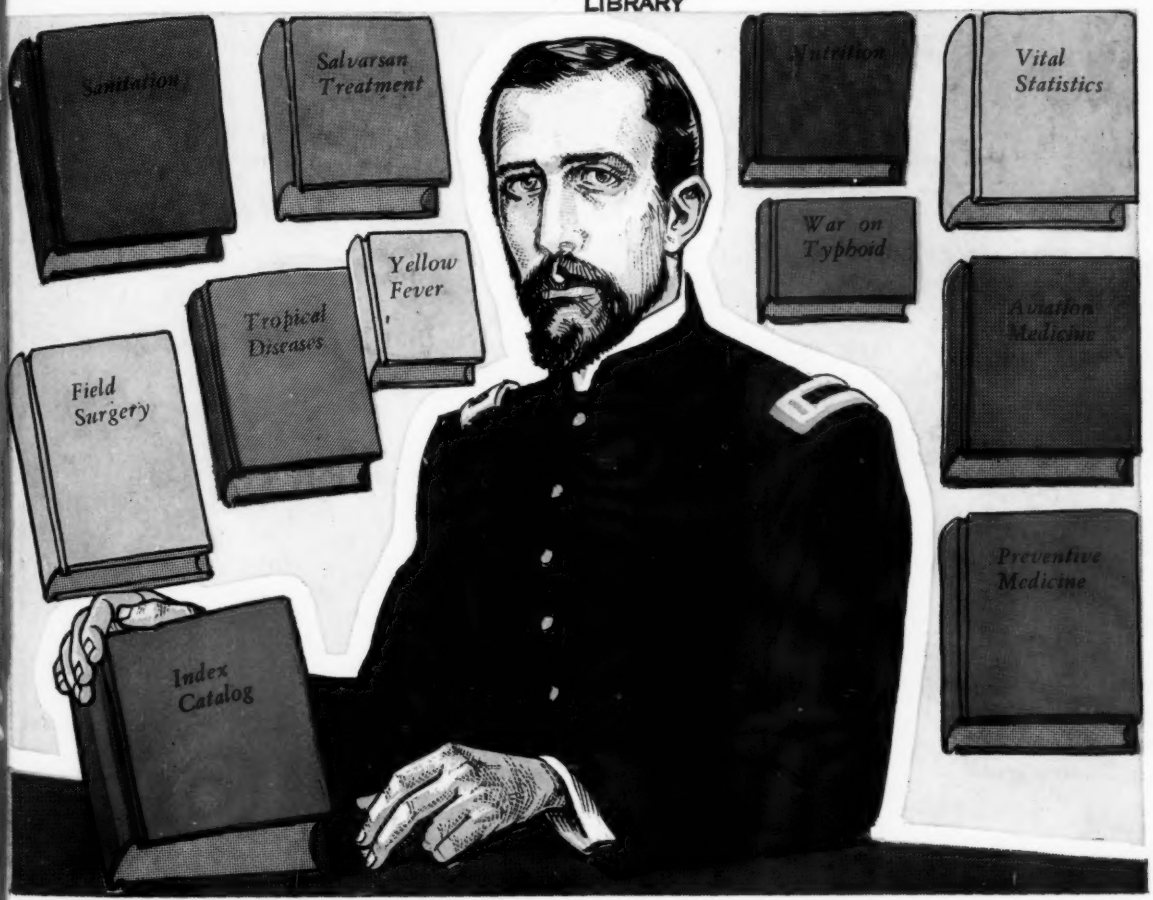

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Medical

Chronic Constrictive Pericarditis: A Practical Discussion

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The diagnosis of constrictive pericarditis is frequently confused with that of mitral stenosis as well as other diseases. This paper presents clues for the early recognition of constrictive pericarditis by clinical and instrumental methods with illustrative cases. The indications for and the use of pericardiectomy as a cure are discussed.

CHRONIC constrictive pericarditis is an uncommon disease that is amenable to cardiac surgery. It therefore behooves the clinician to be aware of and alert to this condition. In most cases the cause is uncertain or obscure. Tuberculosis may be demonstrated or a history of acute pericarditis may be elicited. In many instances no antecedent history of any infection can be obtained. At present it is generally conceded that rheumatic fever is not responsible for this condition. It is a disease that is more than twice as common in men as in women and occurs in any age group, but most commonly between the ages of 10 and 40 years.[1]

The disease is slowly progressive and because of its insidious onset may escape early recognition. It is therefore essential that the diagnosis be made as early as possible in order to avoid extensive myocardial atrophy and degeneration as well as hepatic damage. A complete history and careful physical examination are always important, in addition to the use of instrumental methods, in arriving at an early diagnosis.

The earliest complaint is dyspnea on exertion. At this stage the finding of an accentuated pulmonic second sound and/or a reduplicated pulmonic second sound may indicate the presence of increased pulmonary pressure. The absence of any audible murmurs is significant in eliminating a diagnosis of valvular heart disease, although occasionally a systolic murmur may be heard as in many normal hearts. Careful evaluation of these findings plus use of the roentgenograph, electrocardiograph and phonocardiograph will tentatively establish the diagnosis of chronic constrictive pericarditis in its incipiency. The later complaints are abdominal enlargement due to ascites, and peripheral edema. Orthopnea and nocturnal dyspnea rarely occur. The additional clues to a correct diagnosis are the increased prominence of the cervical veins with increased venous pressure, marked hepatic enlargement, low systolic blood pressure and pulse pressure with a paradoxic pulse, prolonged circulation time, fluoroscopic evidence of poor or absent cardiac pulsations, roentgenologic evidence of pericardial calcification and the typical electrocardiographic findings.

Barnes[2] firmly believes that a diagnosis of constrictive pericarditis is not justified unless venous pressure is found to be elevated. Hitzig[3] demonstrated that the persistence of a rise in venous pressure level during right upper abdominal compression, even when the initial venous pressure was normal, was more significant than any other physical finding or laboratory procedure leading to the diagnosis of this disease.

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MORRIS DRESSLER

The clinical findings are the result of a pathologic mechanism involved in "strangulation" of the heart in whole or in part. The basic condition is an inflammatory lesion of the pericardium and epicardium followed by extensive fibrosis and scarring with usual obliteration of the pericardial cavity. The pericardium is thickened (3 to 20 mm.) and tough and at times contains calcium deposits and occasionally pockets of encapsulated fluid between the coverings of the heart. This inflammatory scar tissue constricts the cardiac muscle, thereby interfering with the diastolic filling and systolic contraction of the heart, and resulting in decreased ventricular output. The interference with systolic contraction is due to fixation of the scar to the myocardium as well as myocardial atrophy and degeneration secondary to limited action and the primary infectious process. In some cases the myocardium may be thin and flabby and calcification may extend into it.

THE cardiac silhouette by roentgenography may be small, normal, or slightly or moderately enlarged. In some cases the thickness of the fibrosed pericardium could account for slight enlargement;[4] we believe that in others it may be due to some degree of auricular and ventricular enlargement. White[4] states that the shape of the heart varies from the normal to the mitral configuration with prominence of the left upper border, and in 3 of his cases there was evidence of left ventricular enlargement. Calcium deposits in the pericardium may be found in about 60 per cent of cases but its presence does not always denote constriction. In most cases there is an increase in the supracardiac shadow due to dilatation of the superior vena cava. Fluoroscopy and roentgenkymography[5] may demonstrate the absence or diminution of cardiac pulsations although at times these may be fairly free on both sides of the heart. It is common to observe free pulsations at the apex of the heart and left border with no pulsations at the right border.

The typical electrocardiographic findings are most suggestive and may lead to the diagnosis of constrictive pericarditis in the absence of other confirmatory findings. The QRS complexes are usually of low voltage in all standard leads. At times they may be low in lead I or in lead I and lead III only. The T waves may be low, flat or inverted in all leads or in only lead I or lead II or both. The QRS changes in the precordial leads are less impaired than in the standard leads. T wave changes are usually observed in these leads when present in the standard leads, and depending on their location indicate injury to the epicardial surface of the right or the left ventricle or both. Fixation of the electrical axis may or may not be present.

Wide and notched P waves in the standard leads may be present indicating disease or dilatation of the auricles in the absence of mitral stenosis or congenital heart disease. Widening of the P wave may be due to dilatation of the atria with consequent prolongation of the depolarizing process or to disease within the wall.[6] Notching indicates either irregularly distributed areas of disease or unequal dilatation of the left and right atria. High voltage of P may be attributed to hypertrophy. Auricular hypertrophy, especially of the right side, often causes large biphasic P waves in the precordial leads V_1V_2 (or CF_1CF_2), and is best seen in the unipolar extremity leads in the right arm and left leg.[7] Auricular fibrillation or flutter may occur.

Until the time of the innovation of cardiac surgery, constrictive pericarditis was considered

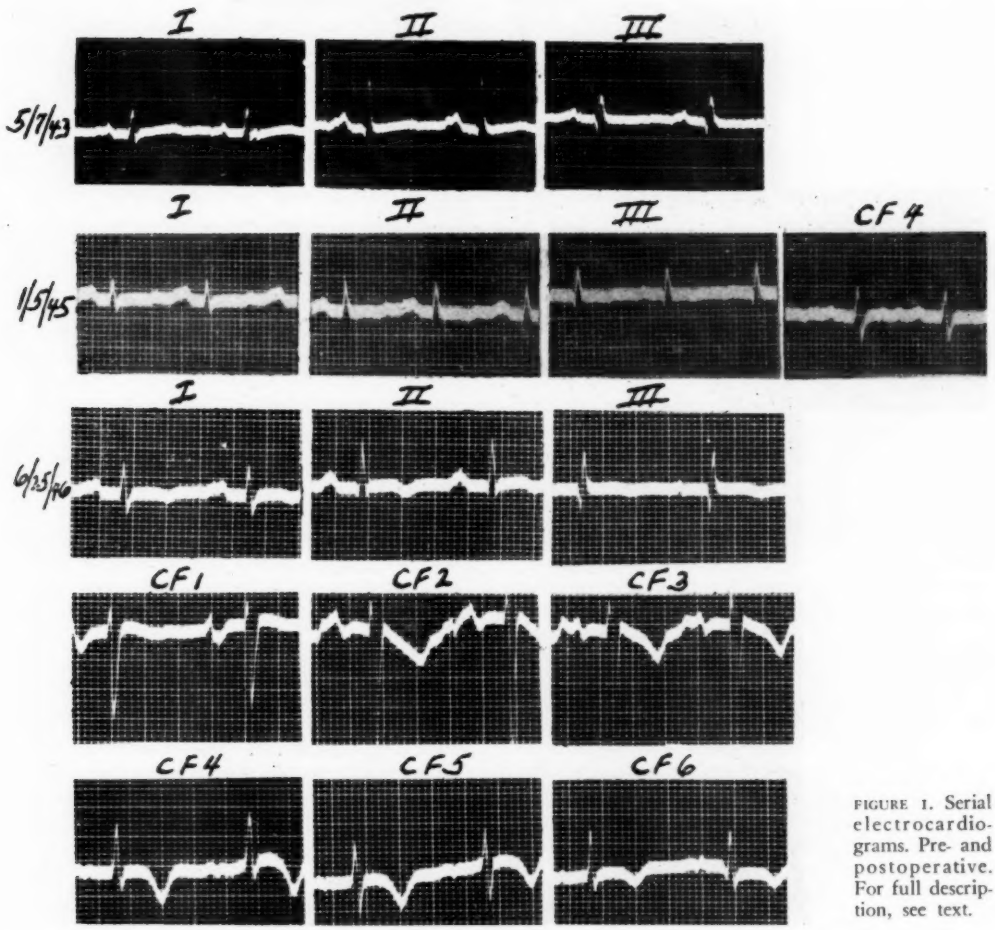

FIGURE 1. Serial electrocardiograms. Pre- and postoperative. For full description, see text.

a hopeless although not a helpless disease. These patients became invalids, bedridden and emaciated, and required frequent paracentesis. With the advent of partial pericardiectomy and epicardiolysis[8] the outlook has changed to that of a real cure or great improvement. Spontaneous cures probably do not exist although remissions may occur with dehydration therapy. White[4] believes that such cures, lasting for months or years after the presence of definite cardiac compression has been established, are due to acute pericarditis with effusion which later recurs as true constrictive pericarditis with pericardial fibrosis.

We would like to report 2 interesting and instructive cases. The first will be presented in full. We are not at liberty to report in detail the second case because this patient is one of a group that has recently been studied elsewhere and will subsequently be reported; nevertheless, we will record some of the important and pertinent diagnostic findings as they compare with our first case.

CASE REPORTS

Case 1—A white army private, single, age 21, was admitted to a military hospital on April 9, 1943, with the chief complaint of fainting spells and dyspnea on exertion. As far back as he could remember he had been having frequent fainting spells associated with nervous-

ness, weakness and breathlessness, and based on this symptomatology he was given a diagnosis of psychoneurosis (conversion hysteria) at another hospital.

His past history revealed measles, chickenpox, pertussis and pneumonia in childhood. There was no history of rheumatic fever (or of any of its manifestations) or tuberculosis.

Physical examination showed a well developed and well nourished young man. The heart percussed enlarged but no significant cardiac murmurs were heard; however, there was reduplication of the second sound at the pulmonic area and at the apex. Blood pressure was 100/70 and the heart rate was regular. The rest of the physical examination was noncontributory.

A roentgenogram was reported as showing widening of the transverse diameter of the heart. Two fluoroscopic studies with barium-filled esophagus showed enlargement of the left auricle and right ventricle. The electrocardiogram (Figure 1) made on May 7, 1943, was reported as showing small T waves and abnormal broad, notched P waves in all leads with normal axis deviation. The other laboratory data were negative.

A diagnosis of valvular heart disease with mitral stenosis was made, and the following comment was recorded by the internist: "There is no question but what this man has organic heart disease. The exact anatomic diagnosis is not certain; however, the presence of a large left auricle and broad notched P waves make a diagnosis of mitral stenosis the most likely, even though a diastolic murmur cannot be heard. The patient's symptoms are functional as evidenced by their character and duration, and are not related to the heart disease."

He was discharged from the army on May 28, 1943, with a certificate of disability.

On January 2, 1945, at age 22, the patient was admitted to the Veterans Administration Hospital, Newington, Connecticut, complaining of dyspnea on exertion, abdominal swelling and edema of the lower extremities. Following his army discharge he had done fairly heavy work without any obvious change in his physical condition until about one year prior to admission when he noticed increasing swelling of the abdomen, swelling of the legs and shortness of breath on walking up a flight of stairs. He was treated by his own physician but his symptoms persisted up to admission to this hospital.

On physical examination we recorded the following: engorged pulsating neck veins; cyanosis; apex impulse not visible or palpable; no thrills or shocks; dullness over the lower sternum; apex percusses in fifth interspace inside MCL; apex does not move with change in position; sounds at apex of good quality but comparatively quiet in proportion to the other findings; pulmonic second sound accentuated and reduplicated; no murmurs heard; pulse small and soft with a rate of 72; blood pressure 90/60; rhythm regular; marked ascites with shifting dullness; enlarged tender liver, and marked edema of lower extremities.

The routine laboratory findings were not contributory. Circulation time showed arm to lung (ether)—8 seconds, and arm to tongue (calcium gluconate)—19 seconds. Venous pressure was 31 cm.

A roentgenogram (Figure 2) with barium-filled esophagus revealed left auricular and right ventricular enlargement. There was irregularity of the outline of the right cardiac border with elevation of the diaphragm due to marked ascites. There was no definite evidence of calcium deposits. Fluoroscopy verified the x-ray findings and failed to show shift of the heart with changing position. There was an increase in the amplitude of pulsations along the left ventricular border with diminished pulsations along the right border and apex.

The electrocardiogram (Figure 1) made on January 5, 1945, showed wide, notched P waves in leads I and II, low voltage of QRS complexes in all standard leads, and slightly inverted T waves in all standard leads and lead CF_4.

The patient received several abdominal paracenteses with repeated intravenous mercupurin injections and a restricted-salt diet.

Following the establishment of the diagnosis of chronic constrictive pericarditis, he was transferred on February 1, 1945, to the Veterans Administration Hospital, Bronx, New York, for cardiac surgery. Our diagnosis was confirmed at this institution and on March 7, 1945, a pericardiectomy was performed. The surgeon found that "the fibrous pericardium was markedly thickened as was the serous pericardium. The pericardial space was obliterated. There was some palpable and visible calcium present. The dissection was made over the major portion of right ventricle, left ventricle, and the base. The left parietal pleura was opened and

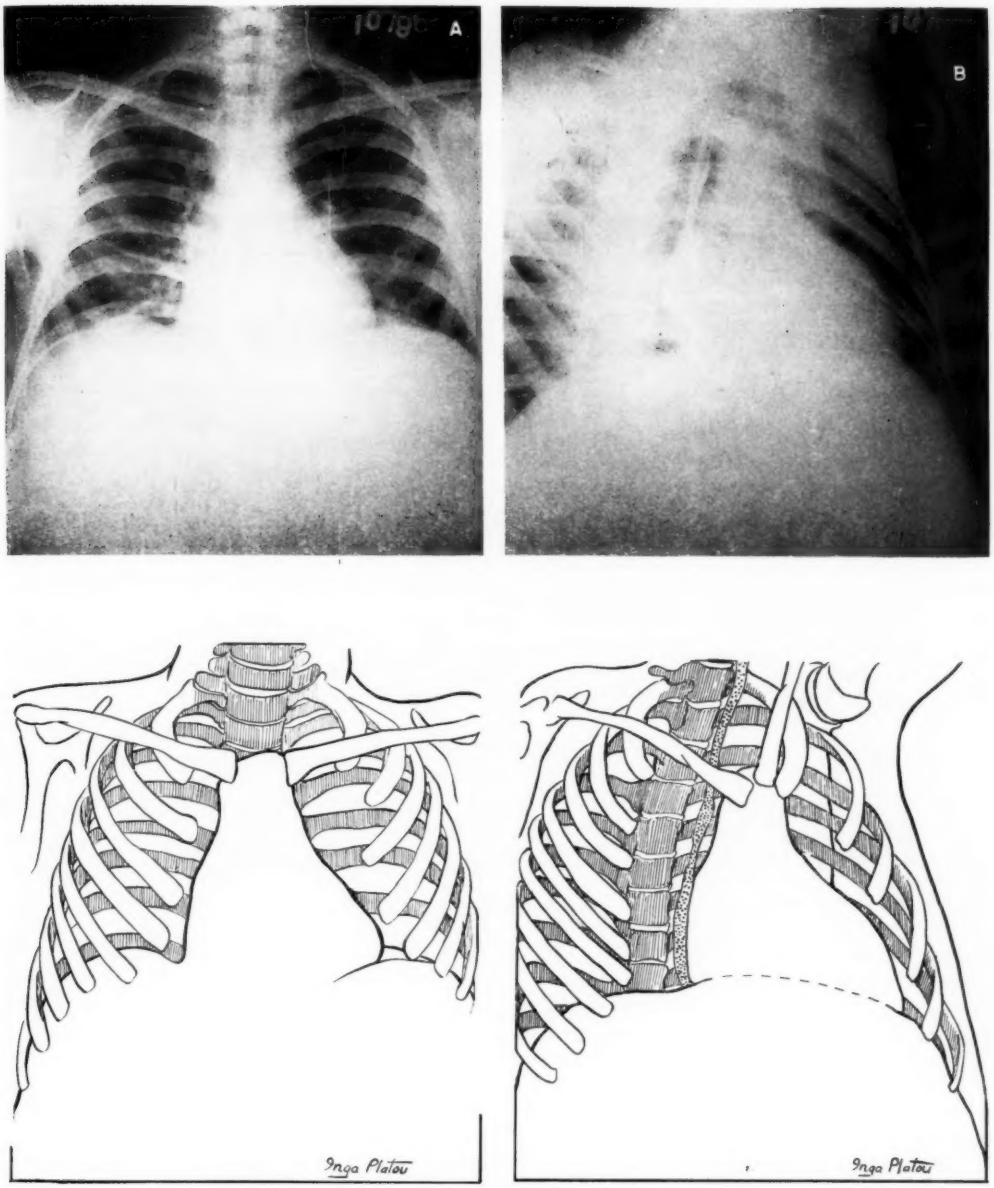

FIGURE 2*a*. (1/5/45) Anteroposterior view. Widening of the cardiac silhouette with irregularity of outline of right cardiac border and some straightening of left upper cardiac contour. Elevation of diaphragm with localized areas of increased density above the diaphragm bilaterally indicating pressure atelectasis at both bases due to marked ascites. *b*. Right anterior oblique view. Prominent bulge of pulmonary conus portion of right ventricle with compression and displacement of barium-filled esophagus due to left auricular enlargement.

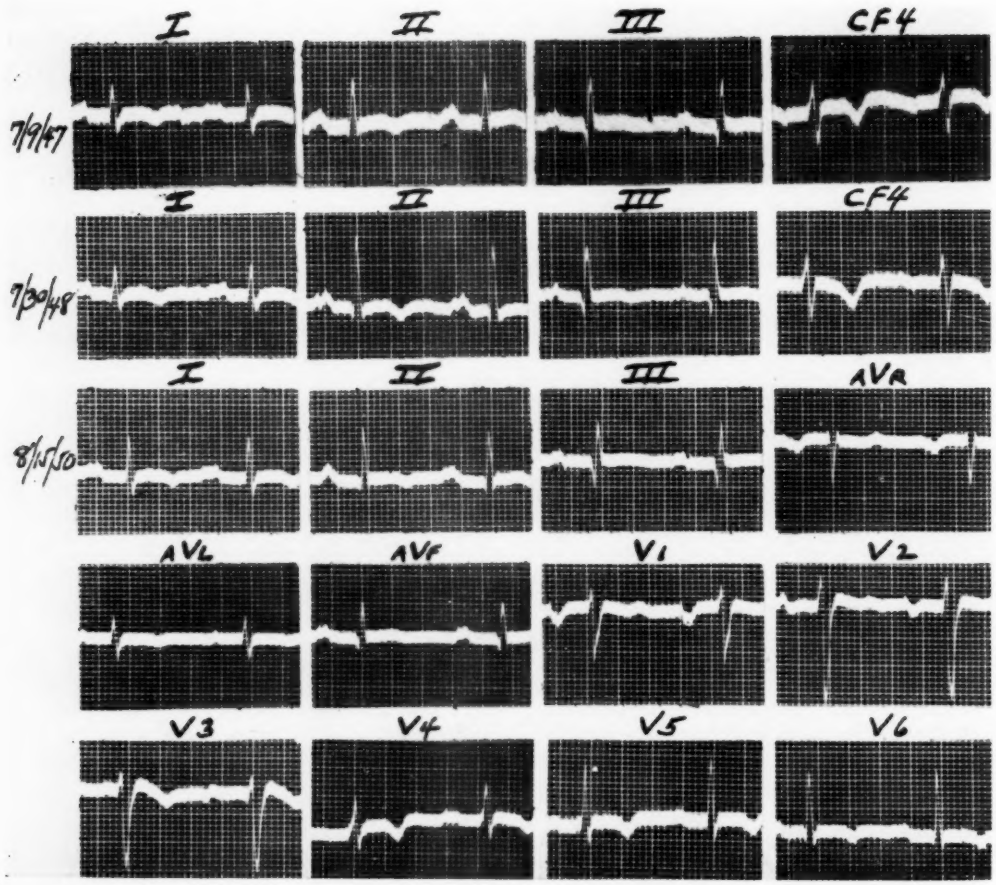

FIGURE 3. Serial electrocardiograms. Postoperative. For full description, see text.

reflected from the pericardium to which it was intimately adherent. The pericardium was dissected from the heart which then bulged through the incision. The pulse pressure immediately increased."

The pathologic findings were reported to be as follows:

1. Gross examination: There are 4 pieces of tissue that average 3.8 cm. by 3.2 cm. by 0.4 cm. There are 4 other pieces that average 1.7 cm. by 1.4 cm. by 0.8 cm., and 3 others that average 1.5 cm. by 0.6 cm. by 0.3 cm. The specimens are smooth and red. One of the larger pieces contains some calcium deposits.

2. Histologic findings: Microsection shows fibrotic tissue. There are no inflammatory cells to be seen.

3. Diagnosis: fibrotic tissue.

Postoperative report dated April 18, 1945, states that "the patient has improved considerably since his operation on March 7, 1945. The dyspnea and cyanosis have disappeared. The ascites is greatly diminished. Patient is active and asymptomatic. On April 6, 1945, the ether time was 2 seconds and the DECHOLIN® time was 19 seconds. On April 9, 1945, the venous pressure was 24 cm. Blood pressure on April 18, 1945, was 100/68." He was discharged on April 19, 1945.

Since the pericardiectomy he has been examined by us once or twice yearly. On February 28, 1946, he was married, and became the father of a son on August 5, 1947.

His first postoperative electrocardiogram (Fig-

ure 1) made on June 25, 1946, showed wide, notched P waves with prolonged P-R interval, normal height of QRS complexes and more deeply inverted T waves in the standard leads. The precordial leads showed large, biphasic P waves in CF_1CF_2 and inverted T waves in CF_1 to CF_6 with upward convexity of ST segment in CF_4, CF_5 and CF_6. Another electrocardiogram (Figure 3) made on July 9, 1947, the following year was practically unchanged. A roentgenogram (Figure 4*a*) with barium-filled esophagus taken on July 30, 1948, continued to show left auricular and right ventricular enlargement. An electrocardiogram on the same day was practically similar to the tracing of July 9, 1947, except that the T waves were more deeply inverted.

At present his only complaints are dyspnea on walking uphill or up a flight of stairs, and fatigue. He owns a small farm which is managed by his wife, and he performs two to three hours of light work per day. He wears a plastic shield over the precordium.

The following is a summary of his last examination on July 18, 1950: A well developed, well nourished man of 27, not acutely ill, appears comfortable. At rest he shows no evidence of dyspnea, no cyanosis, and no engorgement of the cervical veins. Peripheral arteries are normal with a pulse of 72 and a blood pressure of 100/70. Heart shows apex impulse in the fifth interspace outside the midclavicular line. There are thrusting pulsations with each heartbeat over the left anterior chest wall where a small portion of the anterior extremity of the fourth and fifth ribs, the adjacent portion of the costal cartilages and a portion of the adjacent sternum were resected, presenting a sort of skin flap over this area. There are no thrills or shocks and the rhythm is regular. The sounds are distant over the apical area and difficult to evaluate because of the removal of the ribs which acted as a sounding board. The pulmonic second sound is louder than the aortic second sound but is not accentuated. There is a definite reduplication of the pulmonic second sound. No murmurs are heard in any area. The lungs are clear, the liver is not palpable and there is no ascites or peripheral edema.

A roentgenogram (Figure 4*b* and *c*) taken July 18, 1950, showed no gross changes from that of July 30, 1948. An electrocardiogram (Figure 3) taken on August 15, 1950, showed wide, notched P waves with prolonged P-R interval, normal QRS complexes, and inverted T waves in the standard leads. The T waves were less inverted than in the tracing of July 30, 1948. The unipolar extremity leads showed wide, notched P waves in the right arm and left leg. The unipolar precordial leads demonstrated large, biphasic P waves in V_1V_2 with T waves less inverted in V_1 to V_6 as compared with CF_1 to CF_6 in the tracing of June 25, 1946.

Case 2—A 20 year old single white soldier was hospitalized in a military hospital on October 27, 1947, for a hydrocele and right inguinal hernia. There was no history of rheumatic fever, scarlet fever or tuberculosis. The heart was reported as demonstrating a split second sound in the aortic, pulmonic and tricuspid areas. The pulse was 70 and blood pressure 110/80.

He was rehospitalized on December 2, 1947, for a hematoma, postoperative, of the right scrotum. The heart was reported as showing a split pulmonic second sound and a blowing apical murmur. The pulse was 78 and blood pressure 110/78. The cardiac findings were considered insignificant. Unfortunately, no attempt was made to study the heart by fluoroscopy, roentgenography or electrocardiography.

The separation examination from service on March 16, 1948, recorded a functional apical systolic murmur.

He was examined by his private physician on December 19, 1949, and was given a diagnosis of rheumatic heart disease with mitral stenosis and insufficiency, and cardiac failure, predominantly on the right side. Fluoroscopic studies revealed an enlarged left auricle and left ventricle, and the electrocardiogram was reported as showing auricular hypertrophy and myocardial damage. He was given digitoxin, ammonium chloride and mercurial diuretics followed by good diuresis.

On February 28, 1950, at age 23, he was hospitalized. After careful and complete cardiovascular workup, chronic constrictive pericarditis was diagnosed. Phonocardiographic studies showed reduplication of the pulmonic second sound without the presence of any murmurs. The roentgenogram revealed pericardial calcification with left auricular and left ventricular enlargement. The possibility of surgery was considered but it was decided to postpone this indefinitely.

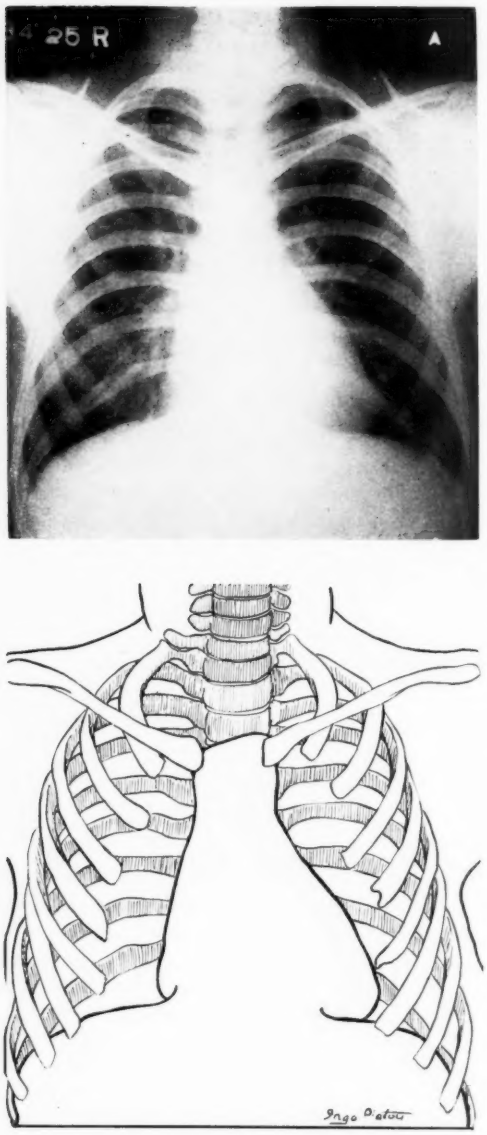

FIGURE 4a. (7/30/48) Anteroposterior view. Widening of cardiac silhouette with straightening of the left upper cardiac contour and prominent bulge of pulmonary conus. Absence of small portion of anterior extremity of fourth and fifth ribs on left with some regeneration of the fifth rib.

COMMENT

Especially in its early stages, mitral stenosis is most frequently mistaken for constrictive pericarditis. The latter condition should be ruled out definitely by the presence of the characteristic diastolic murmur at the mitral area. Establishment by roentgenogram of the presence of pericardial calcification is a definite aid. More attention should be paid to the electrocardiographic findings. In the first case the changes in QRS voltage and T wave tracings were entirely disregarded in favor of the P wave abnormality.

Both cases presented the same early difficulties in arriving at a diagnosis. The belief that left auricular enlargement in the absence of congenital heart disease always connotes mitral stenosis is erroneous. It has been demonstrated that our cases were carefully investigated and no evidence of mitral stenosis was found. Most authors agree that the coexistence of constrictive pericarditis and mitral stenosis is rare. Some believe that cardiac enlargement is due to other types of heart disease. It is our impression that unequal constriction and significant external adhesions (chronic mediastino-pericarditis) may give rise to chamber enlargement depending upon the location of these abnormalities. This is exemplified by marked constriction of the left side of the heart causing left auricular and right ventricular enlargement. Naturally, complete encasement of the entire heart by a contracted fibrous cover with equal constriction will present a small silhouette.

Congestive heart failure should not present undue difficulty in differential diagnosis because of a comparatively shorter history in a much sicker patient, the presence on rest of dyspnea with orthopnea, murmurs or other evidence of underlying endocardial or myocardial disease, and, as a rule, roentgenographic evidence of a markedly enlarged heart with pulmonary congestion.

The enlarged liver which presents abnormal function tests may be confused with primary cirrhosis of the liver, but the presence of elevated venous pressure and distended cervical veins immediately rules out this condition. As pointed out by Paul, et al.,[9] a definite cirrhosis was found in 14 of 16 autopsied cases of constrictive pericarditis. They found that the cirrhosis was not only limited to the central areas (so-called cardiac cirrhosis) but cases with long-standing congestive failure showed portal cirrhosis. They explained this by the fact that chronic passive congestion produces anoxemia

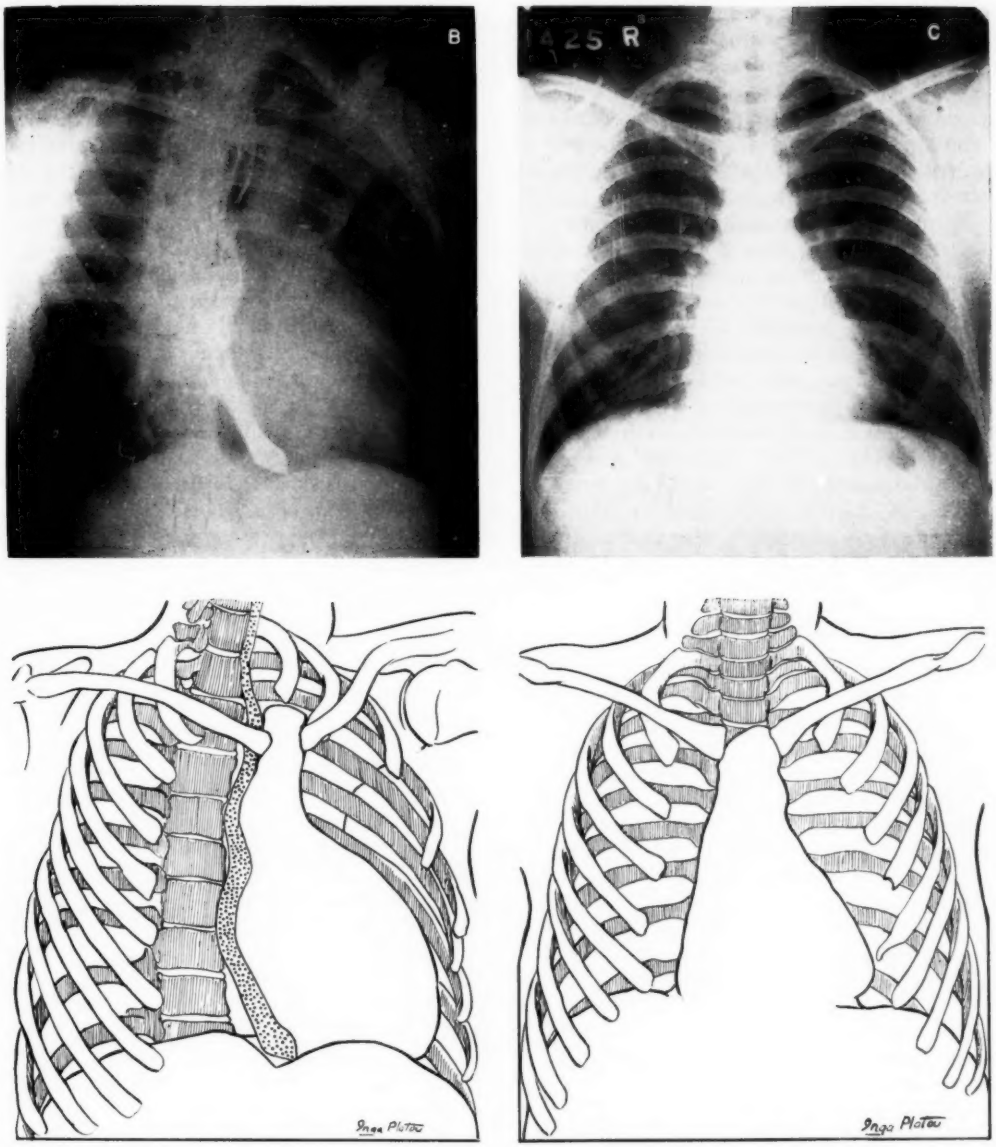

FIGURE 4*b*. Right anterior oblique view. Compression and displacement of barium-filled esophagus due to left auricular enlargement. *c*. (7/18/50) Anteroposterior view. No gross changes from roentgenogram of 7/30/48 except for slight decrease in transverse diameter.

and thereby makes the liver cells anywhere in the lobule more susceptible to injury. They found marked intimal thickening with narrowing of the lumen and in some cases thrombosis with recanalization of the hepatic veins.

Polyserositis, tricuspid valvular disease, nutritional or other edemas and mediastinal tumors are differentiated by the absence of the typical findings of chronic constrictive pericarditis and the presence of their own characteristics.

We feel that more attention should be given the presence of an accentuated pulmonic second sound and/or a reduplicated pulmonic second sound in the early diagnosis of constrictive pericarditis. Paul, et al.,[9] found an accentuated pulmonic second sound in approximately half of 53 patients and felt that it was a significant physical finding.

It must be remembered that in chronic constrictive pericarditis there is essentially a marked inflow stasis due to the inability of the ventricles to expand and fill rather than to the constriction of the veins or auricles.[4] The pathologic physiology[10, 11] shows an increase in the arteriovenous oxygen difference, elevation in the venous pressure, decrease in the cardiac output per minute, decrease in stroke volume and prolongation of the circulation time. Following pericardiectomy the functional capacity of the heart increases in cases that are cured or improved. These tests are of value in diagnosis as well as estimating postoperative improvement.

The question will naturally arise as to the indications for surgery in chronic constrictive pericarditis. It is known that pericardial thickening of various degrees with pericardial calcification may exist without the occurrence of cardiac constriction. External pericardial adhesions of little importance may also exist. One portion of the pericardium may be slightly thickened while another portion, as, for example, that over the right ventricle, may be markedly contracted. We also know that the entire heart may be covered by a tightly constricting encasement. It therefore seems logical to state that surgical intervention is indicated when cardiac constriction exists to a point where there is any interference with cardiac function. If effects of constrictive pericarditis are minimal then surgery may be unnecessary.

On the other hand the presence of hepatic damage and evidence of myocardial degeneration and atrophy require surgery as soon as possible, before the changes in these organs become far advanced and possibly irreversible. Our first case was a typical example of the need for immediate surgery. Of course, it must be remembered at all times that there is a 15 to 20 per cent mortality (decreasing rapidly) with surgery, and therefore all factors should be weighed before a final decision is made. Harrington[8] believes that the percentage of deaths can be decreased by earlier recognition of the disease, which, in turn, would permit earlier institution of surgical treatment.

More than one operation may be necessary because of the incomplete removal of the constricting fibrous tissue or the formation of scar tissue over the defect in the pericardium.[9] An unsuccessful operation may be due to the existence of myocardial disease and the persistence of an active inflammatory process. The recovery of cardiac function following surgery may be a slow process and may require many months, but the ultimate results may bring great satisfaction when it is realized that these patients were hopeless cardiac cripples prior to operation.

Marked changes in the abnormal electrocardiogram do not occur in most cases after operation, even though they are supposedly cured or greatly improved. The persistence of these abnormalities may be attributed to residual epicardial fibrosis and adjacent myocardial damage. Bayley and LaDue[12] have demonstrated in their experiments on dogs that there are no differences in the magnitude or in the kind of electrocardiographic changes resulting from acute local ventricular ischemia and injury, or from local postoperative pericarditis. The electrical effects associated with postoperative pericarditis primarily result from the trauma caused by dissection of the coronary artery and from trauma caused by the sutures used to close the pericardial sac in these experiments.

By roentgenogram, observation at time of operation, or postmortem examination, Paul, et al.,[9] demonstrated pericardial calcification in 29 of 53 cases. Following pericardiectomy there may be no change in size of the heart, or there may be an increase or decrease. In Case 1 no apparent change occurred.

In recent years it has been demonstrated that cardiac catheterization is not only of value in clinical diagnosis of constrictive pericarditis but also is of great help to the surgeon because it has been found useful in localizing the site of constriction. According to White, et al.,[13] if the pressure is increased to a point above normal at the superior vena cava, constriction around the point of entrance of the great vessels, of the right auricle or of the right ventricle should be considered. With a pressure increase in the right ventricle, or even with a normal pressure value and a normal pulse pressure in this chamber, constriction of the right ventricle is ruled out. Right ventricular constriction gives rise to a low

pulse pressure in the right ventricle, and is substantiated by the presence of an accentuated pulmonic second sound. White and his co-authors further state that an increase in pressure at the pulmonary artery indicates the constriction is beyond the right ventricle, presumably in the left auricle and left ventricle.

SUMMARY

1. The important clues leading to both early and later diagnosis of chronic constrictive pericarditis are presented.

2. Instrumental methods such as electrocardiography, roentgenography and phonocardiography are emphasized.

3. Two pertinent cases are described.

4. The criteria for surgical intervention and the value of pericardiectomy are discussed.

5. Cardiac catheterization as an aid in diagnosis and in the localization of constricted areas is cited.

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MEN OF MILITARY MEDICINE

SINCE REVOLUTIONARY WAR DAYS, the Armed Forces Medical Corps has been making important contributions to the general health and welfare of the country as a whole, in addition to its achievements in medical care of military personnel. Some of the principal fields in which outstanding accomplishments have been attained are indicated in this month's cover painting by Edmund Kopietz.

The list of individual men and their work is too long for such a cursory survey but, to mention a few, a beginning can be made with Benjamin Waterhouse who introduced smallpox vaccination; Benjamin Rush, author of the first American textbook on mental disease; William Alexander Hammond, founder of the Army Medical Museum, now the Armed Forces Institute of Pathology; J. J. Woodward, first to use photomicrography in pathology; George Miller Sternberg, pioneer bacteriologist and first to photograph the tubercle bacillus in human tissue; Walter Reed, famed for his work on yellow fever; William Crawford Gorgas, noted for his historic endeavors in yellow fever and malaria control; Henry J. Nichols, who collaborated with Paul Ehrlich in the practical testing of salvarsan, and many others of the past and present.

What has been described as one of the greatest contributions to the science of medicine may be attributed to the imagination and scholarship of John Shaw Billings, originator of the Index-Catalogue of the Surgeon General's Office. Billings joined the medical corps of the United States Army in September 1861. When, in 1865, he took unofficial charge of the Library of the Surgeon General's Office, he started the great task of establishing a fairly complete medical library and the preparation of a comprehensive catalogue and index. Osler described this project by saying, "No undertaking in bibliography of the same magnitude dealing with a special subject had ever been issued, and its extraordinary value was at once appreciated all over the world."

Detection of the Dangerous Paranoid Patient

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Of all patients with paranoid delusions, only some are potentially dangerous and by no means do all of these become assaultive or homocidal. It is important for physicians to be aware of the potential dangers of paranoid patients and it is equally important for them to be sensitive to the signs of a change in equilibrium within the patient which may lead him to become dangerous. This article discusses clues leading to detection of potentially dangerous patients and of potentially dangerous situations, and describes signs of impending danger.

PHYSICAL assaults and homicidal attacks are made by a wide variety of persons under many different circumstances. Dangerous assaults are observed in such conditions as epileptic furor, mental deficiency, psychopathic states with aggression aggravated or released by frustration, alcohol or drugs, and paranoid states. This paper will confine itself to the consideration of paranoid reactions and the clinical manifestations indicating that patients having such reactions are potentially dangerous.

Because there are many paranoid patients who are not dangerous, physicians must be largely responsible for detecting the potentially dangerous ones and arranging for their appropriate treatment. This task obviously is personally important to physicians since their therapeutic endeavors with these patients are so frequently misconstrued with the unhappy result that the helping physician is himself perceived and attacked as an enemy. Clearly no infallible rules of guidance for the detection of the patient who may become dangerous can be made; however, this article will discuss a number of signs which in the past have been found useful by experienced psychiatrists. The subject will be considered under the headings of potentially dangerous patients, potentially dangerous situations, and signs of impending danger.

It is our intention to keep practical considerations in the foreground and therefore no extensive theoretical formulations will be offered. Suffice it to say that the paranoid individual is one who is more than ordinarily isolated from his fellow men. He feels insecure in the real world and protects himself from this insecurity by increasing the distance—physically or emotionally, or both—between himself and others. He overcompensates for his actual insecurity and poverty of experience or achievement by ideas of grandeur and omnipotence of varying degrees of distortion. Consequently he lives in a world of unrealistic self-importance. It generally follows, therefore, that tensions mount within the paranoid person when his isolation is threatened by others' attempts to come close to him or by circumstances which interfere with his system for maintaining self-

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esteem in the presence of actual isolation. It is rare for this isolation to be entirely successful. The patient's suppressed and repressed wishes for affection and closeness unconsciously carry him again and again into situations where he might find satisfying relationships if he could only accept them. His sexual wishes become expressed obliquely through hypochondriacal symptoms. For the relief of these he consults a physician who then must assume the responsibility for detecting a serious illness and possibly preventing serious injuries.

IAN STEVENSON

POTENTIALLY DANGEROUS PATIENTS

THE first clue to the potential danger of a paranoid patient comes from the estimation of the intensity of feeling associated with the false beliefs entertained by him. According to Noyes, "the character and intensity of his emotions will greatly aid in deciding the question as to the hazard entailed in the patient's liberty; the greater the hatred the more imperative is his removal from society. Many times the patient will discuss the extent to which he believes he is justified in protecting himself or his interests or in securing redress. An indication can then be obtained as to the probability of acts of violence."[1]

These remarks apply to the consideration of all paranoid patients. Further guidance may be obtained from the fact that within the general group of paranoid patients some are more often found to be dangerous than others.

Under this heading are to be included patients who have assigned to themselves some special mission in life of a political or religious nature. A great many political fanatics are actually paranoid persons. Not all these persons attain power or use it destructively, but some do, and when they attain great power they may achieve great destruction. Because of the social acceptability of aggression in political and religious matters these persons may continue their activities for many years without being recognized as the victims of a serious illness. But the physician should be attentive when a patient confides in him plans for the fulfillment of a high destiny in political or religious spheres, especially if he shows by his manner or words that for him the ends justify the means.

Outside these spheres, paranoid patients frequently are driven to the protection (by violence) of someone else. They project the feeling of persecution to this other person to whose aid they must then go; for example, the patient may complain that his wife's reputation is being sullied by malicious persons and then decide that he must stop this.

Another group of potentially dangerous patients are those with marked hypochondriacal symptoms, especially of the genital organs or rectum. Such patients are usually expressing their own disguised sexual impulses by these symptoms. At the same time they cannot permit any satisfaction of these sexual impulses from another person and they equate any real or imagined advance with an attack upon themselves. Hypochondriacal symptoms have certain characteristics which should be kept in mind for their more ready recognition. First, they occur without a peripheral physiologic disturbance which might account for them, i.e., they are of central, psychic origin. The physical

ROBERT A. MATTHEWS

examination usually produces negative results or does not fully account for the symptoms. There may be, however, some associated physiologic disturbances which complicate the problem. In these cases the use which the patient makes of the symptoms or his interpretation of them may reveal a hypochondriacal structure around a base of physical disturbance.

A SECOND feature of hypochondriacal symptoms is their occurrence in many, sometimes in all, systems of the body. A third feature is the bizarre quality of the complaints. The descriptions do not resemble the usual descriptions of patients with physiologic changes. Such phrases as "my rectum feels as if something was pushing it," "my ovaries seem dead," and "my stomach seems to be missing" are heard frequently.

A fourth feature is the impossibility of discussing alternative explanations of the symptoms or of offering acceptable reassurance to the patient. He has it all worked out in his own mind and understands more about it than anyone else. These last three features arise from the unconscious symbolic meaning of the symptoms to the patient.

A fifth feature of hypochondriacal symptoms is their use by the patient to establish interpersonal relationships with other people. Illness provides him with an acceptable opportunity for getting somewhat close to people. He is nourished by the sympathy and attention directed to him by doctors and friends interested enough to listen, yet he does not want anyone to come too close and perhaps the very awareness of the professional conduct of the physician makes the latter an ideal partner for such a closely regulated relationship. The physician must remember, when he listens to the unraveling of an account of hypochondriacal symptoms, that his patient's repressed impulses may one day be projected in the form of a suspicion of an attack by the doctor. Suspicion may grow to certainty and certainty to a defensive attitude. When the patient feels defensive he is easily stirred to offensive action.

Because of this constant threat from involvement with paranoid individuals, mention should be made of those paranoid persons who show especial favor or attraction for a doctor or other person. The doctor may feel flattered that he of all others has been able to win approval from such a hostile and rejecting person. Later he may find that he has become the object not only of affection but also of hatred.

A further group of potentially dangerous persons are those whose paranoid trends ordinarily are hidden from casual inspection and are revealed only when the patient's inhibitions are released by alcohol or drugs. Under these circumstances the patient may react with progressively more dangerous belligerence as his drinking (or addiction) continues. We have recently encountered 2 alcoholic patients whose deep and intense hostility to their mothers led to marriages ending in divorce. Under the influence of alcohol, occult paranoid trends became released in these men and they made homicidal assaults on the related women, in one instance on the patient's mother, in the other on the patient's second wife.

In contrast to those paranoid persons who are potentially dangerous, others may be mentioned who are considered less or not at all dangerous. Included in this group are patients who derive considerable satisfaction either from their delusional systems or from their real life situations. Nearly everyone knows persons who harbor systems of beliefs which are completely out of harmony with the culture of the age, but which serve purposes and provide satisfactions for those persons. Also familiar are paranoid persons whose wealth or otherwise protected situations permit them to live in isolation from others. In general, patients with a full development of grandiose delusions are less dangerous than are those in whom this compensatory process has not occurred. Even the delusion of being persecuted may provide satisfactions through feelings of importance which may help the patient to be more comfortable and correspondingly less dangerous. In this respect delusions of persecution are similar to delusions of grandeur.

When the delusional system is largely encapsulated from the rest of the personality there is less danger of physical acting-out. Many persons have a rather elaborate delusional system which is, however, almost entirely isolated from the rest of their psychic functioning. The general functioning of the person in work or social relationships is not interfered with. Either through their own awareness or through therapy, such patients frequently achieve some insight into the abnormality of their beliefs as compared with those general in the culture. They may learn to keep their paranoid delusions to themselves or, if under great pressure, to confide them to a sympathetic psychiatrist.

Finally, mention may be made of the lessened danger in schizophrenic patients who, as their illness progresses, usually show a blunting of the feelings associated with their false beliefs. It is perhaps fortunate that this is the course of illness in the large majority of paranoid personalities. The result is that the patient, although continuing to cherish paranoid delusions, lacks the emotional drive to act upon his delusions.

POTENTIALLY DANGEROUS SITUATIONS

From the foregoing it will be seen that the potentially dangerous situations are those in which the equilibrium of the patient's tension-satisfaction balance is upset. Anything which diminishes the total amount of satisfaction and security enjoyed by the patient provides a potentially dangerous situation. Thus a patient may become noticeably worse after he is fired from a job or fails an examination.

For the most part the circumstances which disturb the balance are beyond the control of the physician, but three may be mentioned further. In the first the physician may be drawn into attempting some therapeutic modification of hypochondriacal symptoms. Without realizing their nature he may proctoscope the patient or operate on him. We would not imply that this is always dangerous, but it may be so. The patient may interpret the procedure as a sexual advance or a mutilation or both.

Another potentially dangerous situation for the physician is that of increasing intimacy with the patient. A genuine wish to help, and the aforementioned flattering notion that the patient really likes him, may lead the physician to make special concessions to the patient. One thing may lead to another until the physician finds that unwittingly he has intensified rather than allayed the antagonism of the patient. The practicing psychiatrist, in his efforts to help these distressed persons, deliberately—and for that reason less dangerously—endeavors to work with them. But his fuller understanding also enables him to watch for the evidence that his relationship is no longer helpful to the patient and is possibly dangerous to himself.

Still another dangerous situation is produced by the sudden withdrawal of support by a physician who has been seeing the patient regularly and who decides, perhaps with good reason, that he can no longer help the patient. The patient may turn against his previous benefactor with hatred for what he feels to be rejection.

This situation is more likely to occur with a physician untrained in psychiatry who first interests himself in the patient and then realizes that he has taken on more than he can handle (or more than he cares to handle). The trained psychiatrist protects himself and the patient, either by never becoming involved with the patient if he is seen to be clearly paranoid at the outset, or by arranging continuing support of some kind if he feels obliged to withdraw from the case.

SIGNS OF IMPENDING DANGER

The patients and situations described in preceding sections are only potentially dangerous. Of all these patients and situations only a small fraction eventually become dangerous. It would be inappropriate and indeed impossible for physicians to act as if such patients were all actually or imminently assaultive to a degree necessitating appropriate hospitalization or supervision; instead, in most instances, physicians must delay such intervention until definite signs of impending danger are noted. Once these are detected, suitable action should no longer be delayed.

In the early phases of a shift in the equilibrium of the paranoid patient leading to a physical attack, a change in the ideas and delusions of the patient is often found. Particular attention should be given to a narrowing of the focus of hostility from many persons to only one. When the patient stops talking about his enemies in general and singles out one of them as the archenemy, he may be near the point of taking positive action based on his delusion. The religious or political fanatic, for example, may decide finally that one person in particular interferes with his plans and must be removed. A serious misinterpretation by the patient of an ordinary, but distressing, event in his life should also be heeded. Thus, when a patient has been demoted or fired from his job and begins to hint that this is part of a larger plot to ruin him which has been planned by a particular individual, he is probably thinking also of doing something about this. Similarly, attention must be sharpened when a patient claims that someone is out to get him or insists that his doctor is giving him poison instead of medicine. There may be a fusion of hypochondriacal complaints and delusions of persecution; for example, a patient who has formerly complained that his blood was rotten may now insist that this is the result of the injections given him by Dr. So-and-So and that he is being slowly killed by these injections. Remarks of this sort to one doctor about another should always be reported to the doctor whose therapy is being woven into the delusional system.

Beyond these changes in ideation are found signs of increasing tension in the patient. He may show increasing agitation and restlessness. His voice may become strained and insistent. The usual physical changes of anxiety probably will be present. The patient may become more demanding and be more frustrated when his demands cannot be met. He may pass into a panic-like state and indeed he really is in a panic with the thought of the attack which he feels is about to be carried out on him and against which he must act defensively through offense. He may request admission to the hospital and this should never be denied to a paranoid patient in this condition.

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Antibiotic and Sulfonamide Therapy in Communicable Diseases

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It is now possible to terminate rapidly many of the communicable diseases and to eradicate complications by the use of the antibiotics and sulfonamides. A group of diseases and their treatment are reviewed, and a bibliography included.

In recent years we have witnessed an interesting and most welcome phenomenon—a reduction in the incidence of some of the common communicable diseases. This has become so general that the need for large communicable disease hospitals is rapidly disappearing. Some of this change has occurred because of the natural evolution of diseases. In many instances, especially in bacterial disease, sulfonamides and antibiotics have accounted for the marked drop in both morbidity and mortality. In the case of viral diseases this drop in mortality is the result of elimination of the secondary invaders through the use of antibiotics or sulfonamides, but none of these drugs seem to exert a direct action on the viruses of poliomyelitis, mumps, influenza, chickenpox, measles and the encephalitides. Likewise none of these drugs exert a direct antitoxic action in cases of diphtheria and tetanus.

In the discussion which follows we shall attempt to point out the treatment of choice of some of these communicable diseases, especially diphtheria, scarlet fever, measles, whooping cough and influenzal meningitis. Brief comment will be made concerning the management of a few of the other conditions.

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DIPHTHERIA

It is well to start with the warning that at the present time we have no antibiotic, no sulfonamide nor any other preparation which can supplant diphtheria antitoxin in the treatment of acute diphtheria. Toxic complications of diphtheria occur even when the patient is cleared of bacilli by penicillin within 24 to 48 hours after onset of the disease. Whenever the diagnosis of diphtheria is considered to be a definite possibility, antitoxin should be given in adequate dosage after taking the usual precautions referable to horse serum sensitivity.

Since 1943 we have found penicillin effective for eradication of diphtheria bacilli from most patients with acute faucial or wound diphtheria and from diphtheria carriers.[1-5] Continued observations over the last seven years have led to the opinion that penicillin in association with antitoxin should be given to all patients ill with diphtheria (Figure 1). In more than 75 per cent of the cases, 300,000 to 1,000,000 units or more of aqueous procaine penicillin,

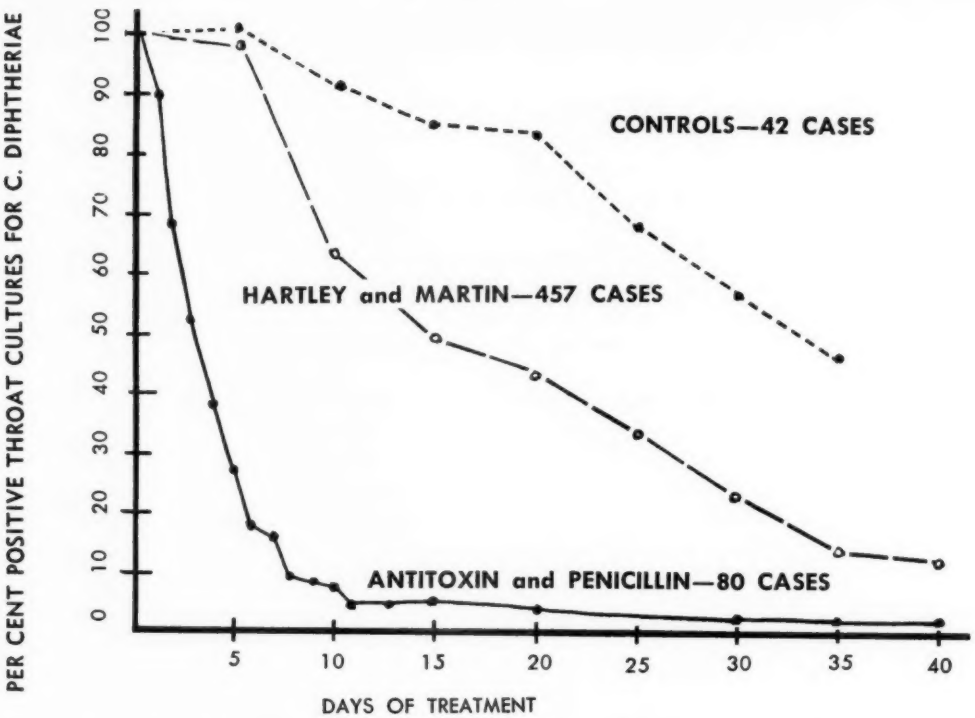

FIGURE 1. Comparison of the results obtained in the treatment of diphtheria with antitoxin alone and with penicillin plus antitoxin.

if given daily intramuscularly, will eradicate the bacilli within a period of time ranging from 12 hours to several days. The penicillin should be continued until at least three negative nose and throat cultures are obtained and, if possible, during this latter period the patient should be removed from contact with patients infected with diphtheria.

SOME strains of *Corynebacterium diphtheriae* are more resistant to penicillin. Doses exceeding 1,000,000 units daily may be required and even these may prove ineffective. Buxbaum[6] and associates found a variation in resistance from ½ unit to over 10 units per cubic centimeter in some 385 strains studied at the Willard Parker Hospital. Others have noted resistant strains in patients receiving as much as 2,000,000 units daily. In such cases tonsillectomy is usually effective.

Penicillin administered locally as nose drops or in nasal or oral aerosol and penicillin troches may be effective in carriers, but we have found the combination of parenteral penicillin therapy and lozenges or nose drops to yield the quickest and most gratifying results.

Aureomycin, 25 mg. per kilogram of body weight, later 50 and 100 mg. per kilogram of body weight per day, has been tried by Karelitz, King and Rubenstein[7] in 24 carriers and active cases of faucial diphtheria. The results were astonishingly good in the first 10 cases. Since then the results have been favorable in acute diphtheria but less striking in the chronically infected carriers. All of the carriers had tonsils. Aureomycin, 50 mg. per kilogram of body weight per day, should be tried in cases of diphtheria which do not respond to penicillin or in patients sensitive to pencillin.

We have observed 1 patient with diphtheritic otitis media and faucial diphtheria whose

pharynx and right ear were also infected with the Friedlander bacillus. Neither organism was eliminated by the daily injection of 900,000 units of aqueous procaine penicillin nor by aureomycin given in amounts up to 100 mg. per kilogram of body weight daily, nor by both drugs given concurrently. Both organisms were eliminated within three days after streptomycin therapy was begun. In vitro studies reveal susceptibility of *C. diphtheriae* to streptomycin but clinical evidence on its use is still scant.

Sensitivity studies with penicillin, aureomycin, POLYMYXIN®, streptomycin, CHLOROMYCETIN® and terramycin (Table 1) reported by Jackson and associates[8] have shown them all to be effective against *C. diphtheriae,* but penicillin, terramycin and aureomycin were found to be the most effective of the nontoxic antibiotics.

In summary, we have found penicillin and, to a lesser degree, aureomycin effective in the treatment of acute faucial diphtheria and diphtheria carriers. These antibiotics in combination with antitoxin are the choice therapeutic agents for treatment of acute diphtheria, and these antibiotics alone are probably the most effective agents for diphtheria carriers. For treatment of secondary infections these same antibiotics are our choice since they are both antidiphtheritic and also are probably the most effective antibiotics for treatment of infections caused by the suppurative bacteria, e.g., streptococcus, staphylococcus and pneumococcus.

TABLE 1

RANGE OF CONCENTRATIONS OF NINE ANTIBIOTICS WHICH COMPLETELY INHIBIT MORE THAN 80 PER CENT OF VIRULENT STRAINS OF *C. Diphtheriae*

ANTIBIOTIC	MINIMUM COMPLETE INHIBITING CONCENTRATIONS, MICROGRAMS PER MILLILITER	PER CENT OF STRAINS
Bacitracin	0.2-0.4	89
Penicillin	0.2-0.8	86
Terramycin	0.8-3.1	92
Chloromycetin	1.6-6.3	92
Neomycin	1.6-6.3	83
Aureomycin	3.1-6.3	83
Streptomycin	3.1-6.3	83
Aerosporin	100-200	92
Polymyxin	200	100

Reproduced through the courtesy of Dr. G. G. Jackson: J. Pediat. 37:718, 1950, and Dr. Borden Veeder, editor, *Journal of Pediatrics.*

SCARLET FEVER

SCARLET fever, like other infections produced by hemolytic streptococci, responds favorably to penicillin, aureomycin and to the sulfonamides.[10-13] There have been controlled studies of the comparative efficacy of penicillin and sulfadiazine in the treatment of scarlet fever, also of the effects of each alone or together as compared with the effects of gamma globulin, convalescent serum or scarlet fever antitoxin.[14-15] The results of most of these studies may be summarized as follows:

Penicillin is the drug of choice in the treatment of scarlet fever. Daily intramuscular injections of 300,000 units of aqueous procaine penicillin or multiple daily doses given orally[16] (for example, 150,000 units of a buffered preparation given every six to eight hours or three to four times a day for 10 days) produced these results (Table 2):

TABLE 2

EFFECTS OF PENICILLIN ON SCARLET FEVER

1. Earlier relief of sore throat
2. Rash unchanged or only slightly affected
3. Temperature normal within three days in over 60 per cent of patients
4. Otitis media, cervical adenitis and sinusitis prevented in most cases
5. Incidence of rheumatic fever reduced
6. Incidence of nephritis reduced
7. Hemolytic streptococcus carriers reduced; recurrent scarlet fever practically eliminated

The rash does not seem to be influenced much, if at all. It does not fade much sooner than in the untreated cases, nor does it disappear as rapidly in patients treated with penicillin or sulfonamides as it does after patients have been treated with gamma globulin, convalescent serum or scarlet fever antitoxin. Otherwise penicillin seems more effective than the antitoxic products. In about 90 per cent of patients in the penicillin-treated groups, the temperature becomes normal within three days. The suppurative complications are prevented; those already present yield to treatment, but a suppurative focus may require more than 10 days of therapy and possibly doses larger than 300,000 units daily of penicillin. In most penicillin-treated patients the upper respiratory tract is cleared of beta hemolytic streptococci in from 24 to 48 hours

TABLE 3

VARIATION OF TEMPERATURE IN RELATION TO TREATMENT AND DURATION OF RASH IN MEASLES
Mean Temperatures — Standard Deviation
(Number of Cases)

DAY OF RASH	CONTROLS	PENICILLIN-TREATED	AUREOMYCIN-TREATED
— 1	only 3 cases	only 8 cases	102.61 ± 0.15 (30)
1st	102.95 ± 0.22 (20)	102.67 ± 0.09 (41)	102.46 ± 0.14 (40)
2nd	102.47 ± 0.14 (36)	101.54 ± 0.17 (41)	101.51 ± 0.17 (40)
3rd	100.88 ± 0.15 (37)	100.45 ± 0.08 (40)	99.85 ± 0.14 (38)
4th	100.29 ± 0.14 (29)	99.12 ± 0.09 (30)	99.21 ± 0.1 (33)
5th	100.53 ± 0.21 (18)	98.87 ± 0.05 (27)	98.70 ± 0.04 (31)
6th	100.01 ± 0.18 (17)	99.14 ± 0.05 (24)	98.49 ± 0.00 (22)

and recurrence of the streptococci is much less frequent if treatment is continued for 10 days and if contact with carriers of the streptococcus is eliminated.[14] Recurrent scarlet fever rarely occurs after penicillin treatment. Nonsuppurative diseases such as rheumatic fever and nephritis are sharply reduced.[17-19] In children with uncomplicated scarlet fever we have had excellent clinical results with daily intramuscular injections of 300,000 units of aqueous procaine penicillin for three days followed by the same amount every other day for three to four doses.

Of a group of 1,650 cases of streptococcal infection in one army camp, half were treated with penicillin and half served as controls. Only 2 instances of rheumatic fever were observed in the treated group, while in the untreated group 17 patients developed rheumatic fever.[18] This is statistically significant and indicates the need for early treatment of hemolytic streptococcal infection.

For the past five years it has been the custom of one of us (S.K.) to give sibling and adult contacts of scarlet fever 1 and 2 gm., respectively, of sulfadiazine daily for 7 to 10 days. No secondary cases of scarlet fever or sore throat occurred, whereas severe sore throat and tonsillitis were quite common before this prophylaxis was employed and occasionally scarlet fever with a rash occurred in the adult contact. (During World War II several epidemics of streptococcal infection were arrested by this form of prophylaxis.)

MUMPS

Neither mumps nor its most common complications, orchitis and meningitis, seems to respond to any of the known sulfonamides or antibiotics; however, in cases of complicating suppurative parotitis and other purulent complications, the effectiveness of both sulfonamides and antibiotics depends on the bacteria present.

CHICKENPOX

Mazursky and associates[21] found no benefit from aureomycin given to 41 patients with chickenpox. However, both the antibiotics and sulfonamides, given either locally and/or parenterally, are useful in cases of secondarily infected chickenpox and in treatment of such complications as impetigo, erysipelas, etc.

GERMAN MEASLES

The disease is usually so mild that none of the antibiotics or sulfonamides are indicated except in cases with relatively uncommon suppurative complications.

MEASLES

As in most of the other virus diseases, there is no convincing evidence that the virus or allergic phase of measles is altered by the administration of antibiotics or sulfonamides. Dowling[22] and Drake[23] have reported favorable results in 9 and 12 cases, respectively, which were treated with aureomycin. In a controlled study, King, Curtis and Karelitz[24] treated 45 children in the pre-eruptive or early eruptive phase with 300,000 units of aqueous procaine penicillin intramuscularly daily for four days. Forty-three such cases were treated for four days with 50 mg. of aureomycin per kilogram

TABLE 4

COMPLICATIONS OBSERVED BEFORE AND AFTER TREATMENT OF MEASLES

TYPE	AUREOMYCIN		PENICILLIN		UNTREATED
	Before	*After*	*Before*	*After*	
Otitis media	2	0	1	1	5
Pneumonia	0	0	0	0	3
Croup	2	0	0	0	1
Tonsillitis	0	0	1	0	1
Purulent conjunctivitis	1	0	0	0	0
TOTAL	11%	0%	4.6%	2.3%	23.2%

of body weight per 24 hours, divided into four equal doses administered every six hours, and 44 cases were observed in which no therapy was given. The results were as follows:

The appearance, intensity, distribution and duration of the rash were not altered by treatment with either penicillin or aureomycin. The cough seemed unchanged except in those patients having pulmonary complications, in whom it improved. The coryza and photophobia were not influenced. The two striking differences between the treated and the control groups were in the duration of fever and incidence of complications. Duration of fever in the penicillin-treated group averaged 2.8 days, in the aureomycin-treated group 2.2 days and in the untreated group 4.2 days after the rash first appeared (Table 3). The complications were observed in 23 per cent of the control group, in 4.6 per cent of the penicillin-treated group before treatment, and in 2.3 per cent of this group after treatment. Complications were observed in 11 per cent of the aureomycin-treated group before treatment and in none of this group after treatment (Table 4).

In sporadic cases of pre-eruptive measles we have used sulfonamides with similar success in preventing suppurative complications. These experiences have led us to the conclusion that, in those parts of the world where measles is frequently complicated by pneumonia, otitis media and other suppurative infections, either penicillin, aureomycin and/or possibly sulfadiazine should be given throughout the course of the disease. This is most important in treatment of infants. Kohn and Koiransky[25] demonstrated pulmonary infiltration in measles in the pre-eruptive and eruptive phases in about 62 per cent of children under 4 years of age. In all probability it is these and other subclinical infections due to pyogenic bacteria in which treatment results in an earlier drop of temperature.

PNEUMOCOCCUS MENINGITIS

THE simultaneous administration of sulfadiazine and penicillin in liberal doses intravenously, orally or by both routes is the treatment of choice.[26, 27] Rarely is intrathecal penicillin indicated[27] but there is little risk in administering 1 or 2 daily injections of 10,000 to 50,000 units diluted in 10 cc. of physiologic saline solution if the disease is very severe or is not progressing well with oral and intravenous therapy alone. Treatment may be stopped five to seven days after the temperature has become normal, the spinal fluid clear of bacteria and after the spinal fluid sugar is 50 or more. Survival has been attained in over 80 per cent of cases but complete recovery without sequelae is less frequent.

Aureomycin, chloromycetin and terramycin are effective in pneumococcus pneumonia, but experience with these drugs in pneumococcal meningitis is scant.

MENINGOCOCCEMIA AND MENINGITIS

In meningococcemia alone or with meningococcus meningitis, best results are reported with sulfadiazine.[28] Approximately 0.1 gm. per pound is given by mouth or parenterally as warranted by the patient's condition. This is continued until three days after the temperature and spinal fluid have become normal. Penicillin and aureomycin are also effective. Penicillin added to sulfadiazine does not seem to yield better results

than are achieved by use of sulfadiazine alone.

In the acute fulminating form, the Waterhouse-Friderichsen syndrome, large doses of penicillin and sulfadiazine and of either adrenocortical extracts such as ESCHATIN® or cortisone are urgently needed. In a recent case of a 10 year old girl with meningococcemia who was pulseless and in shock, 60 cc. of eschatin (adrenocortical extract) helped only slightly. Cortisone, 100 mg. given three times within 24 hours, seemed to help somewhat more. A second child with the same disease also seemed to improve with cortisone. Further experience may indicate that cortisone is preferable to eschatin.

Contacts of meningococcus-infected patients such as nurses, family, and dormitory roommates are often infected. In some army barracks as many as 80 per cent of the contacts were infected; 1 to 2 gm. of sulfadiazine daily rapidly eliminated infection in most of these carriers.[29]

STREPTOCOCCUS MENINGITIS

PENICILLIN and sulfadiazine alone or together are still the drugs of choice and should be given intravenously and by mouth in liberal doses until 7 to 10 days after the temperature becomes normal and the spinal fluid is free of bacteria and is otherwise normal.

INFLUENZAL MENINGITIS

Treatment of this disease has passed through several interesting phases. In most cases sulfadiazine alone cannot be expected to yield good results.[30-32] Streptomycin, 25 mg. per pound or 50 mg. per kilogram of body weight, given in divided intramuscular injections every six hours for five to six days, either alone or with sulfadiazine, is usually effective. In more resistant cases, 25 mg. of streptomycin given intrathecally daily for one or two days may be helpful.[33-37] Sulfadiazine, if included, should be given in dosage adequate to attain a blood level of 10 to 12 mg. Usually about 3 gr. or 0.2 gm. per kilogram of body weight per day suffices. Aureomycin is also effective against *Hemophilus influenzae* and several cases have been treated successfully with aureomycin alone or with sulfadiazine by Chandler and Hodes.[38]

Our personal experience with aureomycin in influenzal meningitis is quite limited. One 3 year old patient was given 50 mg. per kilogram of body weight four times a day by mouth for a total of 200 mg. per kilogram of body weight per day. In addition, he was given 500 mg. intravenously twice on the first day and once on the second day following admission. The oral aureomycin was continued for five days after the temperature became normal and the spinal fluid culture was sterile. This child did very well. Recovery seemed complete.

A second child with moderate disease, age 3 years, was given 200 mg. of aureomycin intravenously twice on the first day and once on the second day. The oral dosage was 25 mg. per kilogram of body weight in each of 4 doses given daily at six hour intervals or 100 mg. per kilogram of body weight per 24 hours. The child improved rapidly but complained of headache for the first five days. The temperature dropped by lysis in six days. Treatment was continued for eight days after the temperature remained at 100° F. or less, yet two days after therapy was stopped the spinal fluid cell count rose from 15 to 500 per millimeter and a culture was again positive for *H. influenzae* bacillus. Streptomycin, 1 gm. daily, therefore was substituted for the aureomycin, resulting in a rapid recovery. Further experience raises doubt as to the advisability of treating patients having influenzal meningitis with aureomycin alone.

Chloromycetin, 200 mg. per kilogram of body weight per 24 hours, given by gavage at intervals of four to six hours in doses of 50 mg. per kilogram of body weight, seems to have become the treatment of choice of many. M. Smith and her co-workers[39] have treated 50 children with chloromycetin alone, achieving recovery in 49.

If one is studying the efficacy of various antibiotics, in the treatment of *H. influenzae* meningitis it may be justifiable to try, for example, large doses of aureomycin by vein and by mouth, or chloromycetin or streptomycin alone. Otherwise even the limited available data suggest that it would seem safer to use a combination of either chloromycetin and sulfadiazine or streptomycin and sulfadiazine. Possibly a combination of streptomycin and chloromycetin may

prove more effective. Specific anti-influenzal serum seems unnecessary in most patients.

PERTUSSIS

Aureomycin has been variously reported as both effective and ineffective in treatment of pertussis. Bradford and Day,[40] Alexander and associates[41] and Wells and associates[42] have demonstrated its in vitro effect while Bell and associates[43] have described rapid elimination of *Hemophilus pertussis* and have reduced the period of paroxysms in children with pertussis. One of us (S.K.) has treated 12 children suffering from pertussis with 50 to 60 mg. of aureomycin per kilogram of body weight per 24 hours and has observed that, in 8 of these 12, striking reduction in the frequency and severity of the paroxysms and in vomiting was accomplished in from 48 to 72 hours. Two children had recurrence three and four days respectively after discontinuing the drug, and further improvement was noted when administration of aureomycin was resumed. The successes were characterized by a milder and shortened course of the disease.

Streptomycin has been found effective by Gordon and Almadon,[46] especially in infants where the condition is complicated by pneumonia, but others have been unable to duplicate these results. At the Willard Parker Hospital streptomycin, given both as an aerosol and intramuscularly, seemed to help younger babies but the over-all results were not decisive.[44,45] Polymyxin and aerosporin have also had their proponents and antagonists.[47,48] The beneficial results do not outweigh the nephrotoxic effect. Chloromycetin is believed by many to be effective and the drug of choice, but here too the results vary and are not always good. Macrae[49] gave 250 mg. followed by 125 mg. every six hours for seven days and found improvement within 12 hours in 4 patients and in 24 hours in 1. Gray[50] recommended the following doses of chloromycetin according to age: up to 1 year: 100 mg. per kilogram of body weight, then 60 mg. every three hours; less than 3 years: 100 mg. per kilogram of body weight, then 125 mg. every three hours; more than 3 years: 100 mg. per kilogram of body weight, then 250 mg. every three hours. These dosages were given for five days and good results were reported.

The drugs of choice are chloromycetin and aureomycin, but both should be given in large doses—50 to 100 mg. per kilogram of body weight per day—and should be continued as long as is necessary to obtain a good therapeutic response. More recently terramycin has also been advocated in treatment of pertussis.[51-53]

Although this paper does not deal with the various immunization serums, it must be added that pertussis immune convalescent serum, gamma globulin made from hyperimmune serum, and rabbit antipertussis serum are considered to be the most effective preparations, possibly more effective than any of the antibiotics. Combination therapy consisting of one of the antibiotics and one of the immunization serums is probably the most effective available therapy for whooping cough.

TUBERCULOUS MENINGITIS

The reported results of the treatment of tuberculous meningitis[54-59] are increasingly optimistic. Recovery of better than 50 per cent of the patients treated is the rule wherever intensive therapy, including simultaneous utilization of streptomycin intramuscularly and intrathecally, PROMIZOLE® or a similar drug and para-amino-salicylic acid, is employed. Those having the greatest experience in the management of tuberculous meningitis stress the need for long-lasting, protracted and uninterrupted therapy.

Streptomycin is given intramuscularly in dosages of from 20 to 50 mg. per kilogram of body weight per day. One and one-half to 2 gm. divided into 2 to 4 injections is the maximum daily dose given to any patient. This is continued for 6, 9, 12 months or longer. The duration of treatment is dependent on the time it takes for evidence of active infection in the central nervous system to disappear, for the temperature and cerebrospinal fluid to become normal, and for the electroencephalogram to become normal or to remain unchanged for several tracings. This usually implies intramuscular treatment for at least two months after the cerebrospinal fluid has become normal.

Streptomycin is given intrathecally in dosages

of 20 to 50 mg. depending on the weight of the patient. For the first 8 to 10 days, 2 intrathecal injections are given by some, but 1 daily instillation is more commonly employed. These injections are continued daily for 30 to 60 days, after which they are given once every two days for as long as it takes the cerebrospinal fluid to become normal, and for two weeks thereafter.

When promizole or some equivalent drug is given along with streptomycin, the results are said to be better than with streptomycin alone. (When given for some time, promizole may stimulate breast and thyroid enlargement and growth of pubic hair.) The drug is given by mouth in dosages of 100 mg. per kilogram of body weight per day.

Para-aminosalicylic acid (PAS) has been found to reduce the development of resistance of the tubercle bacillus to streptomycin. It is given in dosages of 0.3 to 0.5 gm. per kilogram of body weight per day by mouth, divided into 4 to 8 doses, and is continued for three to four consecutive days after which it is omitted for one to two days. This cycle is resumed throughout the course of streptomycin therapy.

The intrathecal introduction of tuberculin has been recommended by Drs. Smith and Vollum,[55] who have observed improvement in patients who did not progress well on other forms of therapy. It is too early to judge the results of this addition to the treatment already outlined. If one wishes to add tuberculin to the combined form of therapy, it is advised that reference be made to their publication.

COMMON COLD

Since the common cold is primarily a viral infection, the sulfonamides and antibiotics should not be expected to be effective. Indeed, it is a common experience in hospital wards for children who are receiving penicillin, aureomycin, chloromycetin, terramycin and sulfadiazine, either each alone or in combination, to develop all the signs and symptoms of the common cold or even influenza. Nevertheless, since secondary bacterial invaders rapidly complicate the common cold, producing otitis media, cervical adenitis, or sinusitis and pneumonia, one may introduce these drugs with good results. If facilities for taking nasopharyngeal cultures are available, the demonstration of the presence of pathogenic bacteria such as pneumococcus or the hemolytic streptococcus or *H. influenzae* bacillus is an indication for treatment with the sulfonamide or antibiotic known to be most effective against that particular bacterium.

If *cervical adenitis* develops, energetic treatment is indicated—not only for the duration of the fever, swelling and tenderness of the gland, but for several days thereafter. The same is true for *otitis media.* Treatment must be continued for at least several days after all evidences of ear infection have disappeared. Should there be a recurrence of otitis within a week, the treatment must be more energetic and should be continued for at least 7 to 10 days after all manifestations of ear disease have cleared. If mastoid tenderness or other evidence of mastoid involvement develops, it may be necessary to continue treatment for as long as four to six weeks or possibly longer to obtain complete healing. In the cases of both cervical adenitis and otitis media, penicillin is the drug of choice. In resistant staphylococcal infection, aureomycin added to the penicillin produces more rapid results. If Friedlander bacillus is the infecting agent, streptomycin yields the best results.

Acute sinusitis requires the same intensive antibiotic and sulfonamide therapy as do otitis media and cervical adenitis. In addition, penicillin in the form of nose drops, liquid spray or even as inhalation therapy might be added. Steam inhalations should be employed as ordinarily indicated.

Prophylaxis: The sulfonamides and antibiotics have been used in prophylaxis against recurrences of acute rheumatic fever, the pulmonary complications of fibrocystic disease of the pancreas, and in cases of repeated acute upper respiratory disease. One-half to 1 gm. of sulfadiazine given daily during the fall, winter and spring seasons has reduced the incidence of secondary attacks of rheumatic fever by about 60 per cent. In such cases any infection of the upper respiratory tract must be treated as intensively as if infection with hemolytic streptococcus were present, since that is the only organism stimulating recurrences of the disease.

In cystic fibrosis of the pancreas 50,000 units

of penicillin 3 times daily as an aerosol has reduced the incidence of pulmonary complications appreciably and has thereby extended the life expectancy of these patients. The addition of aureomycin or other drugs as indicated by the bacterial flora is very helpful. In cases of frequent upper respiratory infections the same prophylaxis as is given to rheumatic patients may be utilized. Since many of the upper respiratory diseases are of viral origin, very good results should not be expected; nevertheless, it may be worth trying in specific instances.

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General Anesthesia for Dental Surgery

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General anesthesia for oral surgery is needlessly dangerous when less than 20 per cent oxygen is employed. The technics described, employing safe oxygen concentrations, are universally applicable. The trichlorethylene series is not large enough for definite conclusions.

In recent years increasing numbers of oral surgeons have become aware of the possible danger to brain and heart tissue when hypoxia or anoxia accompanies general anesthesia. Medical anesthetists have been extremely critical of the usual nitrous oxide technic, and justifiably so, but they have offered no satisfactory substitute. Most dental procedures are of brief duration, and it is generally believed that the average patient can well tolerate lowered oxygen tensions for a few minutes. Expert nitrous oxide anesthetists can produce anesthesia again and again with little or no clinical evidence of cerebral or cardiac damage. However, should satisfactory technics be made available, these same experts should be expected to give safer anesthesia if at least 20 per cent oxygen were included in their anesthetic mixtures. In addition we must always bear in mind the fact that the extraction of a diseased tooth does not warrant even subclinical damage to the nervous or the cardiovascular system.

In July 1949, interns and residents from the Section on Oral Surgery began to serve from four to six months with the Section on Anesthesiology in order to learn basic principles of general anesthesia and to familiarize themselves with the pharmacologic properties of the various general anesthetic agents. This program has been extremely beneficial to both services. It has acquainted each with the problems of the other and has stimulated search for technics applicable to oral surgery allowing the administration of at least 20 per cent oxygen with all anesthetic mixtures.

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AGENTS

Cyclopropane, chloroform and ethyl chloride are not used in either the office or clinic. It is our opinion that the rare occurrence of cardiac arrest encountered in cases in which these drugs are used is too grave a potential complication to warrant their use for tooth extractions. Nitrous oxide, PENTOTHAL SODIUM®, VINETHENE® and trichloroethylene (TRILENE®) are used either

alone or in various combinations. Rectal anesthesia with AVERTIN®, SECONAL® or pentothal is useful as basal anesthesia in children but is not particularly adaptable to office practice except for the occasional "problem child." Ether is not satisfactory except when used with the open drop technic for very small children, because of the prolonged induction and recovery time, the irritation from the vapor and the high incidence of nausea and vomiting.

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PREOPERATIVE PREPARATION

Patients with arteriosclerosis, severe hypertension or cardiac disease are hospitalized and receive a regular medical and surgical preoperative work-up. Those with other medical conditions, such as diabetes or renal disease, undergo a medical consultation and are treated in the office if their conditions do not particularly interfere with their daily activity.

Middle-aged patients and those with histories suggestive of medical diseases should have at least a preoperative examination of the heart and lungs. The blood pressure of every patient should be recorded. In doubtful cases it is better to postpone general anesthesia until further data can be obtained or a more complete examination made. Few patients will die from an oral condition, but patients can and do die in dental offices from an unwisely-administered anesthetic. It must be remembered that there is no such thing as a "minor" general anesthetic.

PREMEDICATION is usually omitted in office patients, since barbiturates, opiates and atropine may interfere with judgment or function in the ambulatory patient. If time permits, children are usually premedicated with a barbiturate given orally in a dosage of 100 mg. per 50 pounds of body weight. To be effective, the barbiturate must be given at least one hour before anesthesia is induced.

The occasional large, powerful male patient can be made more manageable with from 50 to 100 mg. of DEMEROL®, given *very slowly* intravenously over a period of three to five minutes. The effects of the intravenous demerol will ordinarily have disappeared after 45 minutes, and the patient can then leave the office alone. No food or liquid should be ingested during the four hour period preceding anesthesia. This fasting period should be extended to six hours for food when sodium pentothal is to be used.

ANESTHETIC TECHNICS

Nitrous oxide and oxygen—All our experience has been with the McKesson dental anesthesia machine, using the following technic: (1) The oxygen concentration is set at 20 per cent and the nitrous oxide concentration at 80 per cent; (2) the exhalation valve is left free, with no pressure; (3) the rebreathing bag is left wide open, for emergencies, although the rebreathing technic is not used; (4) the pressure regulator on the machine is used as a flowmeter and is opened sufficiently (usually to somewhere between 10 and 20 mm. of mercury) to allow a rapid flow of gases.

The patient is asked to hold the nose mask in position during the few moments when other preparations are being made. A low flow of gases (2 to 4 mm. of "pressure") during this period acts fairly well as premedication. The

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bite block is placed before anesthesia is induced, since relaxation is not usually achieved with this anesthetic mixture. The mouth is covered with a detachable mouth mask. Anesthesia is then induced by increasing the flow of gases until the exhalation valve on the nose mask stays open even during inspiration. The high flow of gases prevents air from entering the system, and if the pressure at the exhalation valve is left at zero, the pressures resulting from these high flows will not be transmitted to the patient.

Most children and many placid adults will become unconscious within one to two minutes. At this time the mouth mask is removed and a well placed mouth pack inserted. The success of the anesthesia depends upon the skill with which the nose mask is held in place and the expertness of the positioning of the mouth pack. A pack placed too far back in the pharynx will obstruct respiration. The patient will become cyanotic and then waken, since he is breathing neither oxygen nor nitrous oxide. A pack placed too loosely will allow air to enter the system and anesthesia will fail.

Restraining straps are used on adults and on children if needed. These are put in place after anesthesia has begun and before the operation gets under way.

This type of anesthesia is contraindicated in the presence of severe hypertension, arteriosclerosis and cardiac or cerebral disease, since patients become rather tense under this light anesthesia.

Nitrous oxide, oxygen and vinethene—Most adults and some children will not obtain satisfactory anesthesia with nitrous oxide (80 per cent) and oxygen (20 per cent). Vinethene added to the mixture in concentrations of 1 or 2 per cent will almost always "smooth out" the induction and maintenance of anesthesia. Vinethene is an ether substitute, about seven times as potent as ether, characterized by rapid absorption and elimination and producing excellent analgesia in low concentrations. When used as an adjuvant to nitrous oxide and oxygen, recovery time is not appreciably prolonged over that of nitrous oxide-oxygen alone. Vinethene is explosive in concentrations exceeding 1½ to 2 per cent and should not be used in the presence of cautery or open flame. If used with the non-rebreathing technic, there is little chance for a fire or explosion unless it is used for several hours in small, closed rooms.

Vinethene can also damage diseased livers and kidneys if used alone for periods exceeding 20 or 30 minutes, if the patient becomes hypoxic or if anesthesia is carried to the deeper planes. As already stated, when used in low concentrations as an adjuvant to mixtures containing 20 per cent oxygen for procedures lasting less than one hour, the danger of such complications is negligible.

IMMEDIATELY preceding anesthesia, some vinethene is poured into the vaporizer which is now available for the McKesson anesthesia machine. From 10 to 20 cc. is sufficient for the average two to five-minute extraction. Nitrous oxide and oxygen are then begun as described. After 10 or 15 breaths of the gas mixture, the vaporizer is set at about "one-quarter." Vaporization is increased by one-quarter to one-half a mark every two or three breaths until the patient is unconscious. The mouth mask is re-

moved, the pack placed and surgery begun. Once the surgery is under way, the vaporizer may be gradually shut off, and after 5 or 10 minutes the work can usually continue under nitrous oxide and oxygen alone. It never has been necessary to set the vaporizer above the "five" mark, and the highest mark ordinarily reached is about "three" with adults and from "one and one-half" to "two" with children. The vaporizer is marked from "one" to "ten."

The patient is ready to leave the dental chair after two or three minutes and can leave the office 5 or 10 minutes later.

Sodium pentothal, nitrous oxide and oxygen—Sodium pentothal in 2 per cent solution may be used in place of vinethene to supplement nitrous oxide and oxygen. The barbiturate provides transient basal anesthesia with only slight prolongation of recovery time. From 5 to 10 cc. is injected intravenously over a period of 30 to 60 seconds immediately prior to induction with nitrous oxide (80 per cent) and oxygen (20 per cent). Occasionally, a patient may require small amounts of vinethene during induction. This technic, though rather cumbersome, is very satisfying to nervous patients and to those with a fear of "the mask." The patient is usually amnesic after the injection, with little recollection of the rest of the induction. If the venipuncture is skillfully performed with small-gauge hypodermic needles, the patient frequently requests this pleasant induction for future anesthetic procedures.

The patient can leave the dental chair within a few minutes. If there is no one to escort him home, however, he must remain in the office or recovery room for a half-hour or an hour, since sodium pentothal can interfere with judgment for some time after the effects have apparently worn off.

Sodium pentothal is contraindicated when there is a history of asthma and must be used with caution in the presence of chronic bronchitis. The drug can precipitate an asthmatic attack in susceptible patients, and those with chronic bronchitis may suffer an attack of severe spasmodic cough.

Sodium pentothal—Sodium pentothal has become very popular for dental anesthesia in recent years. If used expertly, it is probably the safest and, to the patient, the most satisfying agent available. However, if used inexpertly, it can be very dangerous. It should never be used by anesthetists who are unable to recognize and treat respiratory arrest and laryngospasm and who do not have the moral courage to stop the anesthesia when the patient does not react properly.

Under sodium pentothal anesthesia, vomitus, blood or saliva touching the vocal cords may provoke a severe and occasionally fatal spasm of the vocal cords. A slight overdose of the drug may bring about respiratory arrest. Respiratory obstruction in the deeper planes may be fatal, since the patient in these planes will not struggle for air (this type of quiet exitus has occurred in dental offices). While these complications are rare, they do occur, and the anesthetist untrained in the proper technic has no right to subject ambulatory patients to these potential dangers for a simple extraction.

Sodium pentothal has the peculiar property of producing complete amnesia in extremely light planes of "anesthesia." It is this "amnesic" plane, rather than the surgical planes, which is used for dental surgery. The patient may be moving, crying out and even talking to the surgeon, but if the eyes are not focusing properly there will be no memory of the procedure. Dreams are not common. While in this "amnesic" plane, patients can swallow, cough and even expectorate. Should vomiting occur (although vomiting is extremely rare when pentothal is used, it is rather dangerous when it *does* occur), the bite block is left in place, the patient is leaned forward in the chair so that his head is just above the knees, solid matter is removed manually from the mouth, the tongue is grasped and pulled well forward, and the patient will then take care of his own airway.

If more than 20 cc. of a 2 per cent solution of sodium pentothal has little effect, it is probably best to begin nitrous oxide and oxygen or local anesthesia or to discontinue anesthesia altogether. This resistant type of patient requires inordinate amounts of the drug and he usually presents a prolonged excitement phase during recovery.

The usual patient undergoing a 5 or 10 minute procedure tolerates sodium pentothal quite well. For induction, 2 cc. of the 2 per cent solution is injected every five seconds until the patient does not answer when spoken to, or until the eyeballs turn upward and outward. Surgery may then begin. The patient will usually move and may cry out, but additional sodium pentothal is not needed for several minutes. It is better for the anesthetist to maintain a strong grip on the patient's head and to talk to him. This induction dose is usually sufficient for the extraction of several teeth. Subsequent injections of 1 to 2 cc. are occasionally necessary, but the "wink reflex" (blinking when the eyelashes are touched) should be maintained at all times.

THE position of the patient is extremely important. We prefer the erect position, since respiratory obstruction is less of a hazard when the chin is well forward and slightly downward, supported by the hand of the anesthetist. The other hand of the anesthetist is placed on top of the patient's head to prevent undue motion. Saliva and blood drain forward and outward, rather than back into the pharynx. Wrists and knees may be restrained with straps after anesthesia is induced. This erect position makes operations on the upper jaw more difficult, but satisfactory work can be performed if the chair is elevated considerably and universal extracting forceps are used.

The recovery period is somewhat prolonged, particularly if more than the induction dose of sodium pentothal has been used. Recovery rooms should be available. The patient should be placed in the lateral position on the cot. If lying on his side, a patient can expectorate more easily and the danger of respiratory obstruction is not present to the same degree found with the supine position.

Patients recovering from sodium pentothal should be watched at all times, since some will act queerly. Black coffee may hasten recovery. It must be remembered that there is postoperative impairment of judgment and that even those patients who apparently fully recover in a few minutes *must be escorted* home, often in spite of their vehement protestations.

In summary, sodium pentothal anesthesia is safe only if the "amnesic" plane of anesthesia is used. Dental surgical technic must at times be altered. Recovery rooms must be provided. The patient must be escorted home or remain in the recovery room for about an hour after apparent full recovery. Extra personnel are required for postanesthetic care. In expert hands, this drug can be the safest agent available for dental anesthesia, since "real" anesthesia is not required. Lack of attention to detail, indiscriminate use and lack of proper protection during the postoperative period will, however, result in grave complications, give the drug a "bad name" with the general public and consequently force limitation of its use even by qualified and trained men.

Vinethene, open drop technic—Vinethene, given by the open drop technic, is particularly useful in children. Induction and recovery are rapid, analgesia is excellent in very light planes of anesthesia, and postoperative nausea and vomiting are not particularly bothersome if respiratory obstruction has been avoided. It is an excellent substitute for chloroform and ethyl chloride, although more expensive than those halogenated agents. The circulatory status is good even at respiratory arrest, and primary cardiac arrest is not a hazard. As with ethyl chloride and chloroform, anesthesia should be discontinued momentarily if there is breath-holding during induction.

Vinethene is approximately seven times as potent as is ether, and continued administration during a period of breath-holding can build up sufficient concentration to cause respiratory arrest should the patient resume respiration with a deep inspiration. Flammability compares with that of ethyl chloride, and flame or cautery should be avoided. The agent is also contraindicated in the presence of liver or kidney disease, for operations lasting more than 20 or 30 minutes and for deep anesthesia. Since relaxation is not required for ordinary dental procedures, deep anesthesia should not be attempted.

The child may be sitting or lying down for the induction. We use both positions but prefer to have the child sitting erect, since children

seem to be more at ease in that position. If induced while lying down, children seem happier in the lateral position with the knees drawn up. It is not necessary to wrap towels about the mask, although they may be used for a minute or two if desired. The vinethene is dropped on a wire frame mask which is covered with six or eight layers of gauze and held over the nose and mouth. The initial drop rate is about 10 drops per minute, and this rate is increased as rapidly as tolerated. It is not necessary to increase the rate past 100 drops per minute. If the child struggles, the anesthetist should talk to him, since many children will obey commands after 15 to 30 seconds. Unconsciousness usually occurs after one to two minutes. It is not necessary to produce full surgical anesthesia with vinethene. The analgesic effect is quite marked in children even though the eyes are open and blinking. Once the child is still, the mask is moved up over the nose, exposing the mouth. An oral pack is placed and the operation begun. From 10 to 20 drops of vinethene per minute are used for maintenance. The bite block is usually placed before induction, if the child will cooperate, but if necessary this can be done after anesthesia is induced.

The same technic may be used in adults but it is not as satisfactory as in children. There is a brief but definite excitement stage, and the dentist with only a technician or nurse to help might not be able to control a large adult.

Rectal sedation—Rectal sedation is occasionally useful in children, especially when combined with firm restraint, nitrous oxide or local anesthesia. Rectal avertin (60 mg. per kilogram of body weight), seconal sodium (1 gr. per 10 or 15 pounds of body weight), or sodium pentothal may be used, although we prefer sodium pentothal. A 10 per cent solution is made by dissolving 1 gm. of pentothal powder in 10 cc. of water (tap water may be used). No more than 1 gm. should be given at any one time. The calculated dose is administered rectally through a small (number 8 or 10 French) urethral catheter. Hypertonic children receive 0.2 cc. per pound of body weight. Placid or obese children usually go to sleep with 0.15 cc. per pound of body weight. The dose for the debilitated child is 0.1 cc. per pound of body weight. After the injection the buttocks are drawn together and held with two strips of adhesive tape. The child is instructed to try to "hold" the solution. If he is not definitely sleepy within five minutes, another cubic centimeter of the solution is injected. If necessary, still another cubic centimeter may be injected after an additional five minutes. The sleepy child is then allowed to rest, with someone watching him for 15 or 20 minutes. After that time, general anesthesia is induced with nitrous oxide or vinethene and the operation performed.

The technic is bothersome and time-consuming and is reserved for the particularly refractory child. Amnesia is complete after the child is definitely drowsy, and psychic trauma is avoided. Future visits to the dentist's office are made with much less resentment and infinitely less noise. Full recovery does not take place for several hours, although the child will move about with stimulation. He can be carried home in about an hour.

Intratracheal technic—Intratracheal anesthesia is used for the more major oral surgical procedures and is reserved for hospitalized patients. The intratracheal tube may be introduced through either the nose or the mouth. If the teeth are to be wired together, the nasal route is most convenient. With severe nasal deformity the oral route can be used, the wires placed and the actual immobilization postponed until the patient has awakened and the tube has been removed.

ANY form of general anesthesia can be used. We prefer a combination of 2 per cent sodium pentothal intravenously, intravenous curare in concentration of 20 units per cubic centimeter, and a 4 per cent solution of cocaine as topical spray. After a few cubic centimeters of sodium pentothal are injected, each nostril is sprayed with cocaine. After several minutes the nasal mucosa will be anesthetized and shrunken by the action of the cocaine. At that time the patient is instructed to inhale deeply several times, and additional cocaine sprayed into the nostrils during inhalation will reach the pharynx and vocal cords. A calculated dose of curare,

usually from 3 to 5 cc., is next injected intravenously. General anesthesia is then induced by injecting 2 cc. of sodium pentothal every five seconds until the patient is asleep. The intratracheal tube is usually passed blindly into the trachea through the more patent nostril, but we do not hesitate to perform the intubation under direct vision with a laryngoscope after two or three unsuccessful attempts with the blind technic.

If the jaws are locked together, a nasal intubation must be performed under topical anesthesia while the patient is awake, since a severe nosebleed in this type of patient might prove fatal under general anesthesia. It is imperative, when intubating under topical anesthesia, to insert a needle into a vein and to inject several cubic centimeters of pentothal *before* cocainization is begun. The barbiturate helps prevent toxic reactions from the cocaine; if a needle is already in place treatment of such reactions is facilitated. The same technic for cocainization is used as already described, except that more solution is sprayed into the pharynx. As soon as the tube enters the trachea, general anesthesia is rather rapidly induced with pentothal, and a small amount of cocaine is sprayed into the intratracheal tube.

The pharynx is now packed with either VASELINE® gauze or gauze soaked in saline. An inflatable balloon attached to the end of the intratracheal tube may be used in place of the pack if the nostrils are sufficiently patent to permit its passage along with the tube. The respiratory tract is now isolated from the surgical field.

Anesthesia is maintained with nitrous oxide and oxygen, supplemented if necessary with small amounts of ether, cyclopropane or pentothal. Cyclopropane must be avoided if ADRENALIN® is used for hemostasis, since severe cardiac arrhythmias may occur.

When the operative procedure is completed, the pharyngeal pack must be removed and the patient turned on his side with the intratracheal tube left in place until he *awakens*. If the tube is removed from a still-anesthetized patient, blood may enter the cocainized tracheobronchial tree. Should the jaws be immobilized, fatal respiratory obstruction may occur if the tube cannot be immediately reinserted blindly or if instruments for tracheotomy are not immediately available. The topical anesthesia, however, has usually disappeared after 45 minutes, and it is almost invariably possible to have the patient sufficiently awake to sit up on the operating table and remove the tube himself.

Trichlorethylene—Trichlorethylene (trilene) is the newest addition to the armamentarium of drugs used to produce anesthesia for oral surgery. It is quite inexpensive as compared with vinethene, and we have recently begun clinical trials using trilene as an adjuvant to nitrous oxide and oxygen. Our experience at the present time is limited to 187 cases. The drug seems to be fully as effective as vinethene, the analgesia is even more remarkable, and recovery time is not prolonged.

If used with 75 per cent nitrous oxide and 25 per cent oxygen, there seem to be no contraindications. It should *never* be used with the absorption technic, since severely toxic products are formed from interaction with the soda lime. It is not very satisfactory as the *sole* anesthetic agent, since cardiac irregularities may occur in moderately deep surgical anesthesia. The technic is the same as that used for nitrous oxide-oxygen-vinethene.

It is our opinion, at the present time, that nitrous oxide and oxygen, supplemented with trichlorethylene, will become the "work horse" for both the clinical and private practice of dental anesthesia.

SUMMARY

THE extraction of a diseased tooth does not warrant the use of anesthetic technics that may produce even subclinical damage to the nervous or the cardiovascular system. The anesthetist must always remember that few patients will die from an oral condition, and that "pushing" an anesthetic agent, or continuing an anesthetic when the patient is reacting unfavorably, is inexcusable, dangerous and unnecessary. General anesthesia for dental surgery need not involve the use of hypoxic mixtures. Technics are available for both office and hospital practice which allow the use of at least 20 per cent oxygen.

SCIENTIFIC EXHIBIT

Migraine

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MIGRAINE is one of the most dramatic forms of chronic headache.

This syndrome presents a difficult problem to the physician because of its frequent occurrence, the severity of the symptoms and the stubbornness with which the symptoms persist in spite of treatment. Although there is little reliable data concerning its frequency, it is estimated that about 8 per cent of the population suffer from this type of headache. Migraine often begins in childhood and about one-half the patients report that their first attack occurred before 15 years of age.

By "migraine" we mean that form of headache which is characteristically unilateral, occurs in bouts usually associated with gastrointestinal or ocular symptoms, is often preceded by visual or psychologic disturbances and is followed by sleep. There is usually a history of similar headaches in the parents or other members of the family.[1]

From the Headache Clinic, Division of Neuropsychiatry, Montefiore Hospital, New York, New York.

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ETIOLOGY OF MIGRAINE

The underlying causes of migraine are at present unknown. Many theories have been advanced in an attempt to explain the development of an attack. The mechanism of the symptoms is, however, fairly well established and may be explained on a vascular basis. The basic factors which cause the dilatation and which alter the sensitivity of the blood vessel and its periarterial plexus are not definitely known. Several concepts have been advanced but the evidence is often meager or lacking in support of such hypotheses.[2]

1. *Endocrine*—Disorders of the pituitary, gonads, adrenal glands and thyroid have all

been suggested as causes of migraine.[3]

2. *Vitamin and dietary factors*—Dietary indiscretion, vitamin deficiency, and low calorific and mineral intake.

3. *Metabolic disturbances*—Toxic, colonic, duodenal and hepatic disorders have all been advanced as being etiologic agents in migraine.

4. *Allergy*—Some investigators favor the theory that migraine is a result of allergic conditions. Also, histamine sensitivity or some other disorder of histamine metabolism has been suggested as a cause of migraine.[5,6]

5. *Metabolite or electrolyte changes*—Fluid imbalance also has been advanced as a possible cause of migraine. Potassium-calcium imbalances have also been suggested.

6. *Heredity.*

MECHANISM OF THE MIGRAINE ATTACK

Recent studies indicate that the mechanism of the headache in all cases of migraine is peripheral, involving the stimulation of pain endings perhaps as a result of vascular changes. In some cases bodily symptoms result from psychologic disturbances.[7,8]

In a recent review we covered some of the newer concepts advanced to explain the vascular changes. The problem of whether or not autonomic changes or imbalances influence disturbances in vascular tone is still undecided. We have utilized arteriography in patients with headaches to demonstrate variations in the size of intracranial vessels. It is our feeling that this method may be useful as an aid in the study of migraine.

At present, most investigators explain the prodromas, course, symptoms, signs and sequelae of the disorder on the basis of changes in the cerebral and meningeal circulation. Proponents of the vascular theory believe that an initial vasoconstriction of the cerebral arteries produces visual and possibly other pre-headache phenomena prior to the onset of the headache.[17] This prodromal period is then followed by dilation and distention of cranial arteries primarily in the distribution of the external carotid artery. It is this arterial dilation with increased amplitude of pulsation that is presumed to cause the headache.

Persistent dilation results in rigid and pipe-like vessels. The pain at this stage is a steady ache replacing the throbbing, pulsating type of the dilated vessel phase. Following this there is a "muscle contraction pain." This pain is a result of the migraine pain and may outlast it. The head pain arises from the stimulation of pain endings which lie in or near the walls of the intracranial arteries, while the muscle pain develops from tension on the nerve endings in the muscle. The realization that the vessel changes cause the symptoms of the migraine syndrome has resulted in more effective symptomatic relief.

DIAGNOSIS OF MIGRAINE

The diagnosis requires careful physical and neurologic examination with ancillary tests such as roentgenologic examination, electroencephalogram, and any other laboratory studies which may be indicated. Efforts to correlate blood, urine, spinal fluid or basal metabolism abnormalities have failed.[9] In addition, it is just as important to study the patient adequately from the psychologic point of view since neither the physical nor the psychologic aspects can be neglected when attempting to diagnose this syndrome.

Probably the most important factor in formulating a definite diagnosis is the clinical history. We have, after many years, arrived at what we feel is a comprehensive history form. It covers all important aspects of a patient's history and reveals important factors necessary for a correct evaluation of the patient's headaches.*

CRITERIA FOR DIAGNOSIS

1. Recurrent headache, usually throbbing and unilateral at onset, occurring against a background of relative well-being.

2. Temporary visual disorders preceding the headache, such as scintillating scotomas, photophobia, hemianopsia and blurred vision.

*Samples of this history form may be obtained on request to the Editorial Department of POSTGRADUATE MEDICINE.

3. Nausea, vomiting and irritability, occurring at the height of the attack.

4. Personality characteristics of inflexibility and shyness in childhood, giving rise to adult perfectionism, rigidity and resentment, ambitiousness and often efficiency.

5. A history of migraine in the immediate family.

6. Less frequent symptoms, such as paresthesias, speech disorders, dizziness, sweating and other vasomotor disorders.

7. Relief by ergotamine derivatives in about 85 per cent of the cases.

The clinical picture of migraine makes it evident that we are dealing with individuals who have a labile physiologic mechanism which makes them sensitive to any emotional stress. During these states such a labile mechanism can set off multiple physiologic reactions which we call the migraine syndrome, the headache itself being the most prominent symptom in a widespread pattern of dysfunction. Due to the variability of these attacks, many names have been attached to these episodes, such as menstrual headache, week-end headache, menopausal headache, constipation headache, histamine headache and atypical facial neuralgia.

DIFFERENTIAL DIAGNOSIS

In any evaluation of migraine it is obviously imperative to differentiate migraine from other forms of chronic headache.

> "We feel that it is important to stress this fact because of the regrettable tendency in everyday medical practice, and to some extent in the medical literature as well, to apply the term migraine to any chronic, recurring headache. While there may well be similarities between migraine and other types of headaches, the similarities are more than outweighed by important differences, particularly in the physiologic mechanism of the individual attack."[2]

The following table lists the various types of headache which may be confused with migraine:

TUMORS
- Neoplasms
- Aneurysms
- Hematomas

TRAUMA
- Post-traumatic encephalopathy
- Post-traumatic psychogenic headache
- Scalp scars and other injuries

INFLAMMATION
- SINUSITIS
  - Frontal, ethmoidal, sphenoidal
  - Sluder's vacuum type
  - Temporal arteritis

ENDOCRINE
- GONADAL
  - Menstrual
  - Menopausal
  - Hypothyroid

SYSTEMIC
- Arterial hypertension
- Anemia

SPECIFIC
- OCULAR
  - Glaucoma
  - Astigmatism
  - Convergence insufficiency
- CERVICAL
  - Myalgia, arthritis, disks, dislocations and tumors
- HISTAMINE
  - Horton's histamine headache

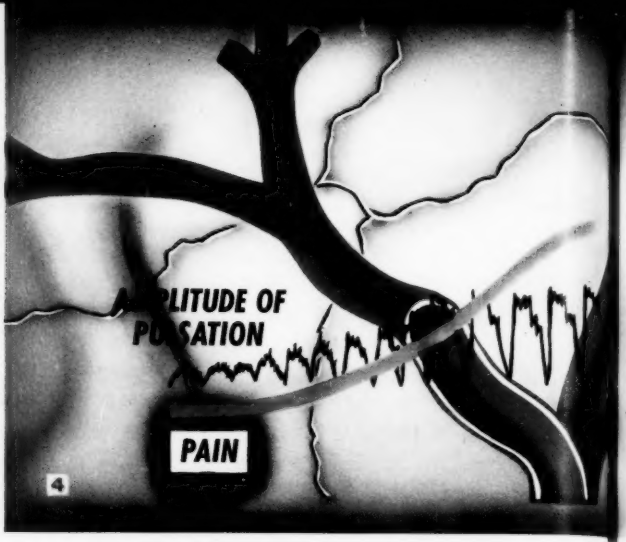
NEURALGIAS
- CRANIOFACIAL
  - Occipital
  - Temporal
  - Trigeminal
  - Ciliary
  - Sphenopalatine
  - Glossopharyngeal atypical facial migraine

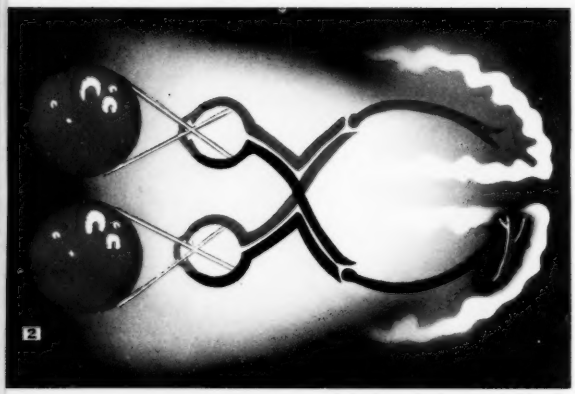
TENSIONAL
- CERVICAL
  - Muscle tension due to inflammation, trauma, etc.
- SCALP
  - Muscle tension due to inflammation, trauma, etc.

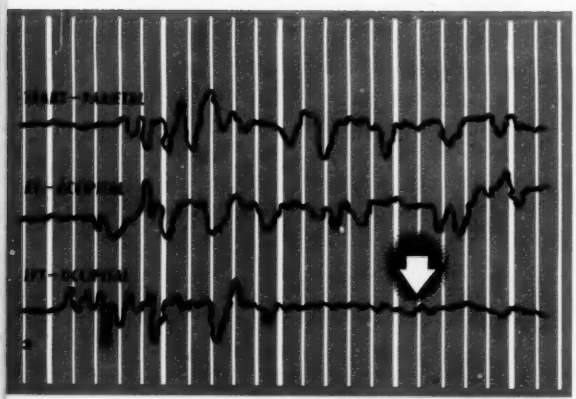
EMOTIONAL
- PHYSIOLOGIC
  - Tensional (muscle) } caused by pain
  - Vascular (dilation) } and/or anxiety
- PSYCHOGENIC
  - Conversion
  - Symbolic

TREATMENT

Our experience indicates that there are two principal modes of therapy for migraine: drug therapy and psychotherapy. Since a twofold







ETIOLOGY AND MECHANISM OF MIGRAINE

FIGURE 1. *Etiology.* Other possible causes may be endocrine, allergic, metabolic, hereditary, and so on.

Pre-Headache

(Vascular Vasoconstriction)

FIGURE 2. *Prodromata:* (1) gastric, (2) psychologic, (3) paresthesia.

FIGURE 3. Electroencephalographic changes in the occipital lobe occurring during visual scotomas.

Headache

(Vasodilatation)

Vascular

FIGURE 4. *First stage:* vessels dilated, throbbing pain.

FIGURE 5. Transmission of pain by the fifth, ninth and tenth cranial nerves and the cervical nerves.

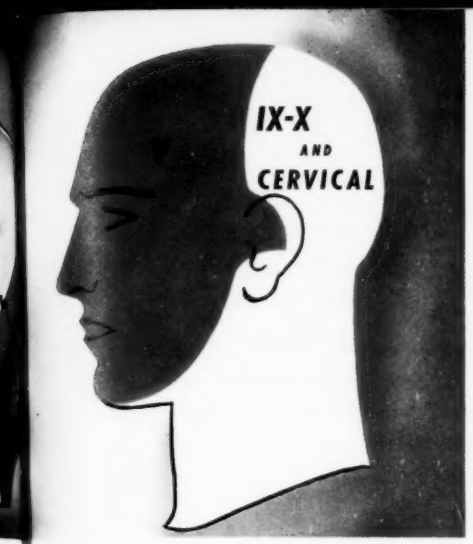
FIGURE 6. *Second stage:* Vessels thickened and edematous; headache continues as steady pain.

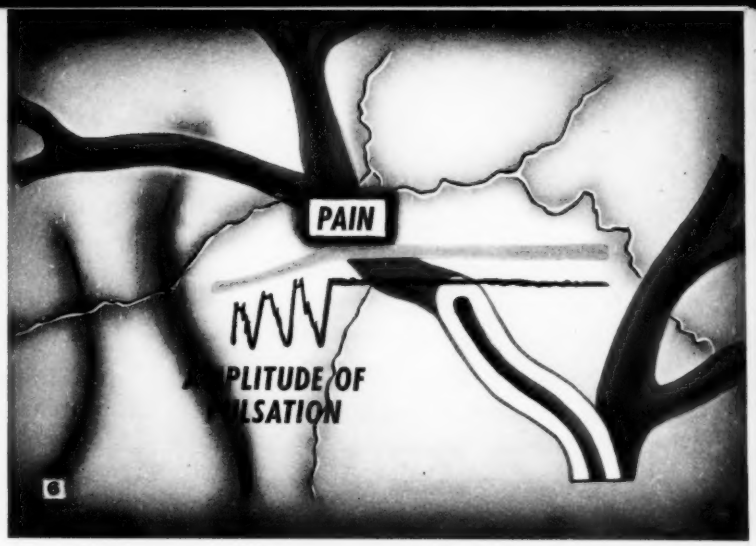
Muscular

FIGURE 7. *Third stage:* Muscle spasm, deep pain.

FIGURE 8. Contraction of the muscles of the head and neck. Pain may outlast original vascular pain.

etiologic relationship exists in migraine patients, treatment must perforce be aimed at both the emotional and physiologic mechanisms. There is abundant clinical experience to prove that





all three types of headache (migraine, post-traumatic or psychogenic) are readily precipitated and made worse by emotional stress and inner conflicts. It is of the greatest importance to bear in mind this apparent but often neglected fact when one is first examining and later treating a patient with chronic headache. If anyone fails to do so, he must pay the price of his neglect ultimately in the form of less satisfactory therapeutic results.[4]

Personality studies have indicated that many patients with migraine are meticulous, neat in appearance, rigid in their thinking and excessively aggressive toward their environment.[10,11] It is often noted that in their earlier life history they have had considerable insecurity with resulting tensions which are manifested in inflexibility, over-conscientiousness, meticulousness, perfectionism and resentment.[4,17] In a recent study[12] it was observed that psychodynamic mechanisms play an important role even in migraine of young children. The types of neurotic symptoms in the children observed were varied and dramatic. They included temper tantrums, numerous phobias, frequent nightmares, hairpulling, enuresis, obvious anxiety, hyperactivity, lethargy, thumbsucking, nail-biting, feeding difficulties, etc.

In migraine, as in other types of chronic headache, a variety of unconscious conflicts and needs may be pathogenic. It appears that emotional factors may very well be an important etiologic factor or "trigger" which sets off the attack of migraine.[13] (However, it is quite likely

TABLE 1

PER CENT OF PATIENTS IMPROVED BY VARIOUS DRUGS AND METHODS

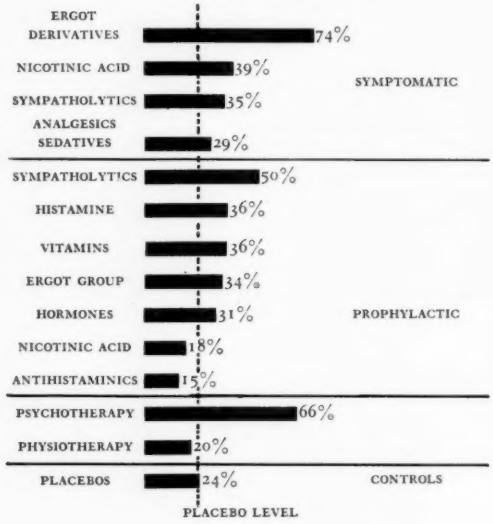
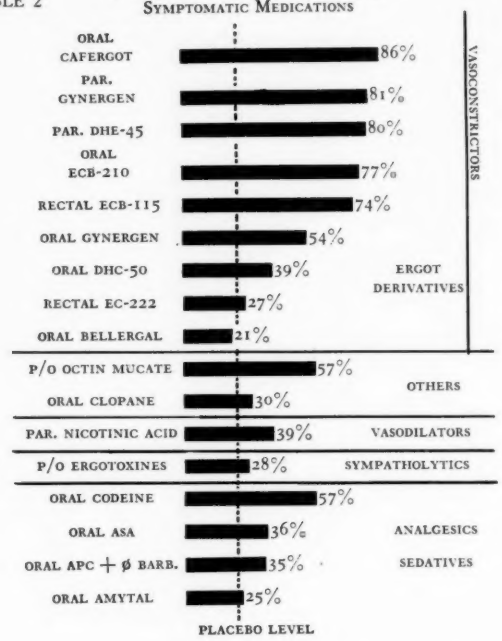


TABLE 2

PER CENT OF PATIENTS IMPROVED BY SYMPTOMATIC MEDICATIONS



that in some patients the trigger may be allergic, endocrine or metabolic in nature.) In addition, it is quite unlikely that a definite "migraine personality" exists, for these personality traits are not observed in migraine alone. In order to obtain best therapeutic results, treatment must give symptomatic relief as well as psychologic help to the patient. The following case taken from our clinic files illustrates these therapeutic principles.[14]

CASE REPORT

G. Z., a male attorney, aged 32 years, had been suffering with attacks of migraine since his graduation from law school four years previous to examination. There was nothing noteworthy on physical or neurologic examination. Ergotamine tartrate was helpful in controlling or alleviating the attacks, but even with its help the patient was not always successful in avoiding severe discomfort.

After some study it was ascertained that the migraine headaches occurred most often the evening before the patient was to appear in court or on a Sunday when he did no work at all. It also became apparent in the course of successive visits that the patient exhibited considerable evidence of psychologic tension.

After a period of psychotherapy and adjustment, the patient became able to attend court without precipitating any attack, and to enjoy his holidays. The frequency of his attacks was markedly reduced; they became of shorter duration and were now invariably relieved by the use of ergotamine tartrate.

SYMPTOMATIC TREATMENT

Many agents have been employed in the treatment of the migraine headache. Our reports are in accord with current opinion that the ergotamine group is unequalled in the symptomatic treatment of migraine (Table 1). As indicated in Table 2 the most effective medication for relief of a migraine attack is the oral use of CAFERGOT® (combination of 1 mg. of ergotamine tartrate and 100 mg. of caffeine alkaloid).

It should be noted that, on preliminary trial,

other vasoconstrictors, such as OCTIN,® mucate and clopane, were useful in only an occasional patient. Our results with vasodilators, nicotinic acid, sympatholytics (D.H.O. 180 and C.C.K. 179) and simple analgesics indicate that these drugs are not very helpful.[2] This, of course, is commensurate with the mechanism of the migraine attack. Since the painful phase of the migraine attack is produced by tension on the nerve endings by the distention of the arteries involved, it follows that the best medication is an agent which constricts the vessels efficiently.

The therapeutic effect of ergotamine tartrate depends on the ability to prolong vasoconstriction. To obtain optimum results care must be taken to give an adequate dose as early as possible after the onset of symptoms. This is particularly important in oral medication with cafergot. Some patients derive greater benefit from parenteral medication with ergotamine tartrate or with D.H.E. 45. Another form of medication with which we have obtained good symptomatic relief is rectal inserts. These rectal inserts, containing ergotamine tartrate and atropine, are most helpful to patients in whom gastric upsets are a prominent symptom.

CONTRAINDICATIONS TO ERGOTAMINE MEDICATION

1. Peripheral vascular diseases
2. Hypertension
3. Coronary diseases and angina pectoris
4. Impaired hepatic or renal function
5. Pregnancy (except D.H.E. 45)

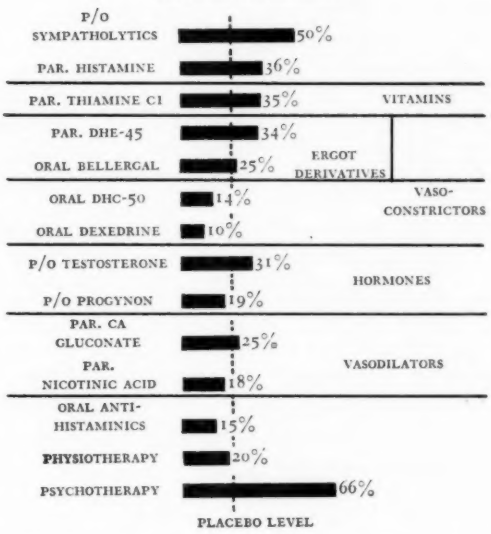
PROPHYLACTIC THERAPY

We can conclude from Table 3 that attempts to prevent migraine attacks are less successful than are the results obtained in symptomatic treatment.

Psychotherapy was effective in 65 per cent of those treated. Such therapy, as practiced by our group, consists of analytically oriented interviews by trained psychiatrists, without, however, any attempt at formal analysis. Maintenance of improvement by psychotherapy has been sustained over periods of two to four years. A large number of these patients will respond satisfactorily to the type of psychotherapy which is well within the province of the general practitioner.[2]

TABLE 3

PER CENT OF PATIENTS IMPROVED BY PROPHYLACTIC METHODS



Prophylactic therapy with sympatholytics holds some promise. The use of D.H.O. and C.C.K. has resulted in the prevention of migraine in 50 per cent of the cases in which this therapy was used. However, these results are based on observations of no more than a year's duration. Histamine desensitization has not been too successful in our hands. Although a definite clinical entity known as histaminic cephalgia is recognized,[19,21,24] our feeling at the present time is that migraine is not a result of histamine sensitivity or of any other disorder of histamine metabolism.

Other prophylactic measures such as nicotinic acid, thiamine chloride, testosterone and antihistaminics have been of little value. Results with physical therapy were unsatisfactory. We have resorted to certain surgical procedures in selected cases in which vascular disease does not allow specific treatment.[15,23] Migraine patients on physical examination do not show any pathology of the head or neck. Roentgenologic examinations do not reveal any cervical lesion which might produce migraine. In our

clinic, therapeutic trials with cervical manipulation were of little use in the treatment of migraine. In addition, we have seldom observed any post-traumatic cases to develop migraine.

COMMON CAUSES OF THERAPEUTIC FAILURE

1. Incorrect diagnosis
2. Inappropriate, inadequate or improper administration of medication
3. Inflexibility of therapeutic regimen
4. Failure to recognize the variable etiology of the syndrome
5. Additional factors associated with the migraine attack
6. Inadequate patient-physician relationship

FOR BETTER MIGRAINE THERAPY

Flexible, individualized treatment—*not* a rigid, universal regimen.

Consideration of { variable / accessory / complicating } factors in each case.

More intensive, deeper-level psychotherapy.

SUMMARY AND CONCLUSIONS

1. Migraine is a complicated syndrome which may present, in addition to the severe, throbbing, unilateral head pain, ocular, gastric and psychologic symptoms.

2. Complete physical and laboratory examinations in addition to a thorough history are necessary prior to reaching a diagnosis.

3. Migraine must be distinguished from various other headaches in order to assure good therapeutic results.

4. Treatment must include drug therapy (symptomatic) as well as psychotherapy (prophylactic).

5. Best symptomatic relief is obtained with an oral preparation combining ergotamine tartrate with caffeine.

6. Psychotherapy is effective in reducing the number and severity of the attacks. The patient must be taught how to live with his problems and must learn to achieve the proper balance between work and play.

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Fibrosarcoma of the Extremities

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Fibrosarcoma is the most common important tumor of the extremities. The pathologic aspects of these tumors, which are important from the clinical point of view, are the pronounced tendency toward invasion into surrounding mesenchymal tissue, a pronounced tendency to recur unless radically excised, and the danger to the patient of recurrence and vascular metastases. Radical excision of the tumor without attempting to dissect away its attachments is the minimal surgical procedure. Recurrence of a sarcoma after an attempt at local excision is an indication for amputation.

KLEITSCH

MALIGNANT tumors of the extremities are usually mesenchymal in origin, and fibrosarcoma is by far the most common. These tumors are slow-growing and painless and follow a deceptively benign course, often for several years. Then, quite suddenly, pulmonary metastases develop and the patient rapidly succumbs to the disease. The published material on the subject of fibrosarcoma is not particularly helpful to the clinician who must treat these patients, because most investigators have concerned themselves with statistical surveys rather than with applying their findings to individual cases. A statistical survey helps to understand the disease; it does not necessarily indicate proper treatment. The statistical and pathologic study of fibrosarcomas of the extremities, by the authors indicated in the bibliography, has elicited certain important facts which permit the clinician to develop a scheme of treatment.

This study was prepared in an effort to derive a sound and rational approach to the treatment of fibrosarcoma occurring in the extremities of individual patients. Rather than surveying all our cases, we have selected illustrative case histories to demonstrate the conclusions we have reached. We have attempted to illustrate how to treat the patient who develops a fibrosarcoma in one of his limbs rather than to repeat the excellent studies of this disease accomplished by other authors.

*From the Surgical Service of the Veterans Hospital, Omaha, Nebraska, and the Creighton University, School of Medicine, Department of Surgery. The cases cited are from the files of the Veterans Hospital in Lincoln, Nebraska.

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CLINICAL PATHOLOGY

Much of the confusion about the subject of fibrosarcoma has been produced by a failure to appreciate the implications of its pathology. At-

tempts at detailed classification and grading of these tumors have produced little of clinical value. From the point of view of the clinician who must treat this disease, the more simple the classification the more effective will be its clinical application. As a matter of fact, the clinician is best advised to consider all malignant mesenchymal tumors to be mesenchymomas, without becoming involved in their more specialized features. As suggested by Willis, a simple and effective method is to consider all malignant soft-tissue tumors of the extremities to be derived from fetal mesenchyme. Such tumors can then be understood to have the potentiality of differentiating into the various mesenchymal organs and forming smooth muscle, bone, cartilage, nerve, fat, fibrous connective tissue, etc. The type of differentiation of the tumor is of no clinical significance since they all behave the same and all must be treated in a similar manner. The only clinical significance of subclassification of mesenchymal tumors of the extremities is that the fibrosarcoma is the most common. The inclusion of other mesenchymal elements in a fibrosarcoma has no implications relative to treatment or prognosis in the individual case.

Burke attempted to develop a system of grading fibrosarcoma similar to the one developed by Broders for carcinoma. His prognostic standards, however, are not generally accepted. As far as histopathologic grading is concerned, the only consistent finding is that the more cellular tumors *usually* have a poorer prognosis. Tumor giant cells are significant only in that they are most commonly found in the more cellular type of tumor and, therefore, may be said to be associated with a poorer prognosis. Even this, however, is not universally true.

The single most important prognostic feature of sarcoma of the extremities is the clinical course of the disease. If a patient remains apparently cured for a year after excision of a sarcoma, his prognosis—although still guarded—may be said to be good. If the tumor recurs within a year after excision, the prognosis—although still guarded—is poor. When a sarcoma has recurred after local excision, immediate amputation must be considered to be the treatment of choice. Recurrence of a sarcoma must always be viewed with the greatest concern, regardless of the histologic appearance, and it is best interpreted as an indication that local excision is futile.

The clinical course of fibrosarcoma differs from that of carcinoma in many important respects. To carcinoma-conscious individuals the course of fibrosarcoma is deceptively benign. The fact that the nodules are painless and seldom produce functional impairment keeps the patient from seeking early medical advice. Because the tumor is slow-growing and nonulcerated and only seldom involves the regional lymph nodes, the attending physician is lulled into a false sense of security. This sense of security in the presence of fibrosarcoma is best dispelled by studying published five year survival rates. In 474 reported cases we found a five year survival rate of 17.7 per cent (Table 1).

TABLE 1

SURVIVAL RATE FOR FIBROSARCOMA OF THE EXTREMITIES (474 REPORTED CASES)

AUTHOR	NUMBER OF CASES	FIVE YEAR SURVIVAL
Bick	24	8
Meyerding, et al. ..	152	24
Warren and Sommer	62	13
Carroll, et al.	35	7
Burke	201	32
TOTALS	474	84 (17.7 per cent)

The outstanding malignant feature of fibrosarcoma is its pronounced tendency to local infiltration. The infiltrative nature of the tumor is such that often it is difficult, even by histopathologic study, to identify its margin. The invasiveness of sarcoma applies primarily to mesenchymal tissue. It invades epithelium only late in its course, and skin involvement is usually secondary to pressure or interference with the blood supply. However, because of their invasiveness in mesenchymal tissue, sarcomas are peculiarly prone to form tumor emboli. The sarcoma invades the wall of the blood vessel, invades the intravascular thrombus which forms and finally is disseminated through the vascular tree as a tumor embolus. It may even grow as an actual

"tumor thrombus" within the vascular lumen. This accounts for the rapidly fatal course of the disease once a blood vessel has been involved. There is no system of classification or of grading which will permit one to estimate which tumor is more prone to involve the blood vessels. In fact, it appears that vascular invasion by a sarcoma is a purely fortuitous circumstance which depends upon local factors of growth and proximity rather than on any inherent characteristic of the tumor itself.

TREATMENT

The safest treatment for a sarcoma of the extremities is a high amputation. If all sarcomas of the extremities were treated by early and high amputation, the curability rate of the tumor would undoubtedly become better than 50 per cent. However, many limbs would be needlessly sacrificed. Moreover, the surgeon is reluctant to recommend amputation for a small, painless, slow-growing nodule. If he does suggest it, it is unlikely that the patient will accept the recommendation. The best compromise would seem to be an attempt at wide local excision at the first operation. This excision must be radical in every sense of the word. The patient should be instructed that local excision will be attempted but that it might result in a functionless extremity or an amputation. This is especially true if the nodule is in close proximity to the major neurovascular elements of the extremity, which is, unfortunately, very common.

During the operation no attempt should be made to expose the tumor or to dissect it off neighboring structures. It should, rather, be removed "en bloc" with a generous amount of normal tissue surrounding it in all directions. These tumors are usually adherent somewhere to blood vessels, tendons or nerves. It is at this point that the surgeon becomes less radical and attempts to dissect the tumor away. To do this is a mistake and will result in failure of the local excision. The involved neurovascular elements must not be dissected away from the tumor, but should be divided at a safe distance from it and removed with the block dissection.

If a fascial sheath or tendon is involved, nothing less than myomectomy is indicated. Attempts at reconstruction of the defect may be made after the tumor has been resected; on the other hand, it is probably a better procedure to terminate the operation with excision of the tumor and observe the patient for at least a year. If, after this period of time, no recurrence has developed, plastic and orthopedic procedures might then be considered to improve the functional potential of the limb.

If the attempted local excision reveals involvement of the vascular supply to the extremity, so that excision of the tumor would result in gangrene, amputation should be done at the first operation. The surgeon should always keep in mind, especially when he is questioning his radicality, that the price of conservative dissection is recurrence, and recurrence results in serious depreciation of the prognosis.

If, in spite of radical excision of a sarcoma, a recurrence does occur, amputation must be resorted to. Repeated excision of a sarcoma of an extremity is extremely dangerous, usually ending with fatal blood-borne metastases. The treatment of recurrent sarcoma of an extremity by less than a high amputation cannot be considered to be adequate cancer surgery. By high amputation is meant amputation above the joint above the tumor. Thus, a tumor in the calf or forearm requires amputation through the thigh or arm, whereas a tumor of the thigh or upper arm will require at a very minimum a disarticulation and more probably a hemipelvectomy or intrascapulothoracic amputation.

The use of radiotherapy for the treatment of a fibrosarcoma is generally conceded to be inadequate. As a class, these tumors are extremely radioresistant. An occasional cellular fibrosarcoma may show a slight response to roentgen therapy, but no one has ever suggested that irradiation should be used as the treatment of choice. Radiotherapy is usually confined to the last therapeutic attempts in an otherwise hopeless case.

CASE REPORTS

Case 1—I. K., a 33 year old white male, was

admitted to the hospital on November 20, 1945, for treatment of a swelling of the right buttock which had been noticed for about a month. When first seen by a physician, it was diagnosed as a hematoma and incised. The wound drained for a week and then healed, although the swelling remained the same. Although the patient felt perfectly well, he applied for hospitalization for treatment of the tumor.

Physical examination was within normal limits except for the right buttock, which was found to be grossly enlarged and somewhat indurated. There was no tenderness on palpation. A two inch, well healed surgical scar was present over the area of greatest swelling. A diagnosis of hematoma was again made, and on November 28, 1945, a tumor mass measuring 40 by 20 by 10 cm. was removed from the region of the gluteus maximus muscle by means of morcellation. Pathologic diagnosis of the removed tumor was myxosarcoma. The postoperative course was uneventful and the patient was transferred to another hospital where 12 x-ray treatments were administered.

The patient was next admitted to the hospital on March 4, 1947, at which time he complained of a recurrence of the tumor of his right buttock. It was not very troublesome but interfered with sitting. Physical examination again was within normal limits with the exception of the right buttock. Here there was a well healed, adherent surgical scar, surrounded by an area of skin which showed a moderate degree of radiation tanning. In the inferior aspect of the scar was a hard mass about the size of an orange, and a second mass about the size of a golf ball was palpable next to it. A diagnosis of recurrent myxosarcoma was made.

On March 7, 1947, a radical excision was done, excising the lateral half of the gluteus maximus muscle and removing the two recurrent tumor masses in one block. However, further exploration revealed a mass of tumor tissue in the thigh, overlying the greater trochanter of the femur and extending downward into the vastus lateralis muscle. This mass of tumor was also removed. Although all evidence of tumor had been removed as far as could be determined, the seriousness of the situation was appreciated and an attempt was made to explain this to the patient. A hemipelvectomy was recommended but was refused despite the serious implications of his disease.

He was next seen on September 28, 1947, when he again had a recurrence of the tumor at the lower end of his previous incision. Hemipelvectomy was again strongly urged but steadfastly refused by the patient. He was given a series of x-ray treatments following which he again underwent operation on October 31, 1947. An extremely radical resection was done, removing most of the gluteal and pyramidalis muscles. Histopathologic study revealed a fibromyxosarcoma, grade 2, which was invading subcutaneous tissue, muscle and nerve. The patient recovered from this operation without difficulty. During his convalescence he was again advised that his only hope for survival was a hemipelvectomy, but he still refused to accept it.

The patient was not seen again until February 2, 1949, at which time a new mass was discovered in the upper portion of the thigh. It is interesting to note that the tumor was apparently progressing peripherally with each recurrent excision. On February 15, 1949, he was again operated on, having again refused hemipelvectomy. At this time the tumor was found to involve the upper portion of the hamstring muscle which was resected almost in its entirety, together with the tumor nodules. Microscopic examination of the removed tissue again showed fibromyxosarcoma.

He next appeared for hospitalization on September 19, 1949. Another recurrence was present in the upper thigh and he was again urged to have a hemipelvectomy, which he again refused. On September 21, 1949, he was operated on, and this time local excision was found to be impossible because of involvement of the sciatic nerve. The patient was awake (having had a spinal anesthetic) and he was informed that the tumor could not be removed without dividing the sciatic nerve and losing the function of the leg. He refused this procedure, and the operation was terminated leaving gross tumor in situ. In the postoperative period the patient was again informed of his prognosis and also advised that involvement of the nerve implied a serious and

painful terminal course. He was further advised that tumor involvement of the nerve meant loss of the function of the leg without a chance for survival. Under these circumstances and, more probably, due to the fact that the latest surgical wound had failed to heal, he consented to consider hemipelvectomy if granted a leave to put his affairs in order.

He was readmitted on February 5, 1950, on a litter, reconciled to hemipelvectomy. He was prepared for the operation and on February 14, 1950, a right hemipelvectomy was done in a final attempt to eradicate the disease. Because of the extensive involvement of the skin of the buttock a long anterior skin flap was necessary for closure. It appeared, however, that the tumor had been encompassed in the amputation. Histologic study of the specimen showed a recurrence of the fibromyxosarcoma previously described. The postoperative course was complicated by a small superficial slough of the anterior skin flap and the development of an acute deep phlebitis in the left leg on the seventeenth postoperative day. In general, however, his progress was very satisfactory. The amputation, however, had been too long deferred and the patient died on June 11, 1950, of massive retroperitoneal metastases.

Comment—This case represents, first, a confusion as to original diagnosis which is so often seen in early fibrosarcoma. It also illustrates persistent mismanagement due to the refusal of the patient to accept recommended treatment. Five recurrences were suffered and four years passed before the indicated operation was finally accepted. Survival for comparatively long periods of time with repeated local excisions of a fibrosarcoma is not uncommon. Unfortunately, however, once a recurrence has developed, local removal—no matter how radical—is seldom possible.

Case 2—W. F., a 54 year old white male, was admitted to the hospital on July 30, 1941, complaining of a lump in the region of his left elbow which had been growing larger during the previous year. Physical examination was within normal limits except for the left arm, which carried on the posterior aspect of the elbow a hard tumor mass the size of a lemon. It was freely movable and not believed to be attached to bone. There was no limitation of motion in the joint. A diagnosis of calcified bursa of the left elbow was made and surgical removal was recommended. On August 6, 1941, operation was performed under local NOVOCAINE® anesthesia. The tumor, which was identified as a bursa, was removed by "peeling" it out. The entire procedure took 30 minutes. The pathologic report was chronic bursitis.

THE patient was readmitted to the hospital on August 3, 1942, complaining of "recurrence of bursitis in his left elbow" which had been noted about two months previously. Physical examination at this time revealed a tumor the size of an orange underlying the previous surgical scar. This mass was very hard, essentially painless and apparently not fixed to the bone. He was re-examined by a surgeon, and malignancy was suspected because the tumor had recurred. On August 10, 1942, the tumor was removed under local anesthesia; the mass was the size of a tennis ball and had not infiltrated muscle or bone. Histologic slides were sent to a consultant pathologist for an opinion. The report was as follows: Inflammatory fibrosis with possible low grade malignant changes. The comment by the pathologist was: "The cytologic picture for the most part is one of inflammatory proliferation; however, the fact that there is such a marked variation in the size of the nuclei and other anaplastic changes in the cells leads us to consider possible early, low grade neoplasm. The lesion should be observed closely for evidence of recurrence."

On November 23, 1942, the patient was operated on in another hospital and a local excision was again done. He was next seen on September 10, 1946, and referred to the hospital with a diagnosis of "chronic osteomyelitis of the left forearm and a possibility of carcinoma of the skin." He stated that he had consulted his private physician on June 3, 1945, at which time a tumor again had been removed from his left elbow, and that following the operation he had received 15 x-ray treatments. This operation followed by six months a second excision of a recurrence in the other hospital, making a total of five excisions in four years.

Physical examination at this time was within normal limits with the exception of the left elbow. Here there was a long scar extending, on the posterior aspect, from about two inches above the olecranon, medially and downward over the medial condyle to about two inches below it. Along the scar numerous nodules, some as large as marbles, were felt. There were no nodules in the axilla and the chest roentgenogram was negative. A local excision was decided upon and on September 23, 1946, the recurrence was again resected.

Approximately two months after operation he showed evidence of ulceration of a blood vessel in the surgical wound when a secondary hemorrhage occurred, and a diagnosis of recurrent tumor was made. On November 27, a guillotine amputation in the medial portion of the arm was done, but infiltrative pulmonary metastases had developed. He was discharged on January 6, 1947, for terminal care and died at home on January 28, 1947.

Comment—In contradistinction to the previous case, this report represents a poor choice of procedure. The early course was complicated by undue attention to the original pathologic report. Recurrence of a fibroblastic tumor in an extremity, regardless of the degree of malignancy on histopathologic study, is sufficient to make a diagnosis of malignant fibrosarcoma and should make amputation a very serious consideration. It is significant that, although by histopathologic study the original tumor was recognized only with difficulty as being malignant, it nevertheless produced fatal metastases when a blood vessel was eroded. This case is an object lesson in the fallacy of repeated local excision of a fibrosarcoma. Although the patient lived for more than five years after the onset of the disease, he had a recurrence about once a year. Eventually, as in most cases handled in this manner, vascular involvement terminated the course of the disease.

Case 3—F. S., a 27 year old white male, was admitted to the hospital complaining of a painful mass in the right popliteal fossa which was first noted in 1948. It had started as a 4 cm. nodule for which he had been advised to wear a knee pad. The nodule slowly increased in size until it measured about 10 cm. in diameter, became painful and impaired the movement of the knee. It was excised on May 1, 1949, and was reported to be a fibrosarcoma, grade 1. Six x-ray treatments were given over the site of the excision. In September 1949 the nodule recurred and four additional x-ray treatments were given. Amputation was advised, and he was admitted to the hospital on January 3, 1950, for further treatment.

Examination revealed limitation of motion of the right knee. There was a healed transverse scar in the right popliteal fossa and radiation tanning of the skin. Beneath the lateral half of the scar was a firm mass about 5 cm. in diameter, densely adherent to the skin and deeper structures. A chest roentgenogram was normal.

On January 4, 1950, an amputation was done through the junction of the middle and lower thirds of the right thigh. The pathologist reported a firm, white nodular mass adherent to the tibial nerve and popliteal artery. Microscopic examination disclosed a typical neurofibroma with interlacing fasciculi, marked anaplasia and scattered mitosis. Careful study of the slide disclosed a thrombus in one small blood vessel, which had become infiltrated with many highly anaplastic tumor cells. The postoperative course was uneventful and the patient was discharged as healed on the fourteenth postoperative day. He was seen two months later and given instructions for preparing the stump to receive a prosthesis. No evidence of recurrence or metastases was noted at this time.

Comment—Here again we find confusion in first establishing the diagnosis. Once the diagnosis was established, however, the treatment was well considered. Nevertheless, after histologic study of the surgical specimen, malignant cells were found within a thrombus in a blood vessel. Therefore, despite the facts that the tumor was apparently of a low order of malignancy and that treatment was of an approved type, the prognosis must remain guarded. However, the patient has now survived his amputation for more than 18 months without evidence of recurrence, and the prognosis might be somewhat more cheerful.

Case 4—W. A., a 21 year old veteran, was admitted to the hospital on January 4, 1950, for treatment of a tumor of his left forearm. He had been aware of a mass in his forearm for a year. In May 1949 he had consulted his physician who treated it with alternate hot and cold packs after having made a diagnosis of "a muscle hernia." On several occasions the doctor attempted to aspirate the mass without success and finally advised hospitalization. On physical examination in the hospital a large mass was discovered "covering the entire dorsum of the left forearm, extending from a point about two inches below the elbow to a point just above the wrist." The mass was semi-fluctuant, which was apparently the reason that it had been needled. A small area of desquamation on the mass indicated the site where an ethyl chloride spray had been used in passing the aspirating needle. The mass was not attached to the underlying bone. Roentgenologic studies of the forearm confirmed the presence of a soft-tissue tumor and revealed small areas of calcification within it. A reactive periosteal and cortical overgrowth was present in the mid and distal portions of the radius. There was no evidence of tumor involvement of the bone. A chest roentgenogram was negative; no metastases were seen.

On January 6, 1950, under brachial block anesthesia, the left forearm was explored and a large tumor was found lying beneath and within the belly of the extensor communis digitorum muscle and adherent to its tendon. The muscle was dissected away from its point of origin and lifted off the deeper structures of the forearm, carrying the tumor with it. The tendons were then divided distal to the tumor and the surgical specimen was removed. The postoperative course was uneventful. The histopathologic diagnosis was fibromyxosarcoma. The patient was supplied with a cockup splint and given physiotherapy.

He was next seen approximately one year after operation at which time the scar was found to be well healed, there was no evidence of recurrence and the function of the hand was almost normal, without reconstructive operations. The patient was recalled for observation and possibly some orthopedic treatment, but in July 1951 it was found that he was on active duty with the Armed Services, the resection of the fibrosarcoma apparently having been successful.

Comment—This case illustrates the ideal treatment of fibrosarcoma with a fortuitous result. Like all malignancies, sarcomas cannot be considered cured until at least five years have passed. However, failure of a recurrence to appear after 18 months suggests that a cure might be hoped for.

DISCUSSION

It is apparent from this study that the clinician is caught in a serious dilemma when treatment of a malignant soft-tissue tumor of the extremity is considered. Excluding benign lipomas, fibrosarcoma is by far the most common important soft-tissue tumor occurring in the extremities. Unfortunately it is a very serious disease, and the clinician must weigh the possibility of an unnecessary amputation against that of a fatal recurrence. The decision is complicated by the fact that incision into the tumor for any purpose, including biopsy, is dangerous and may promote a fatal recurrence. It is made yet more difficult by the fact that the histopathologic picture does not consistently identify the malignancy of the tumor. The local invasiveness of a malignant fibrosarcoma is so great that the borderline between normal and pathologic tissue is often difficult to determine even with the microscope. Fortunately, fibrosarcomas usually can be diagnosed clinically so that biopsy becomes less important than with other types of tumors.

In view of the above-mentioned difficulties it is still possible to develop a rational mode of treatment of these tumors. If the tumor is seen when it is small and confined to a single muscle belly, a radical excision (which usually implies a myomectomy) can be attempted. An essential part of the wide excision is not to dissect away the tumor attachments. It is absolutely imperative that the points of attachment of the tumor be widely circumcised and taken away in the "en bloc" dissection, even though it means sacrificing a major nerve or blood vessel. Functional impairment should not be considered in the treatment until after the primary malignancy has been removed.

Should the surgeon experience difficulty in deciding to make the excision sufficiently radical, he need only remember that the price of conservative excision is recurrence, and recurrence means amputation and/or death. If the tumor is ruptured or morcellated during removal, it is best to consider the local excision a failure, and immediate amputation should be done without waiting for a clinical recurrence. Clinical recurrence of the tumor after local excision is best interpreted as an indication of failure of local excision and an absolute indication for a high amputation.

These tumors should never be irradiated except as a last desperate effort at treatment. It is in only the rare instance that irradiation may retard the progress of the disease. Irradiation of a fibrosarcoma has never been shown to be of value in the control of the disease and may do serious harm by impairing the vitality of tissues which later may require an amputation.

SUMMARY

1. A soft-tissue tumor occurring in an extremity should be regarded as an extremely grave disease since it usually means a fibrosarcoma has been discovered.

2. Extremely radical local excision, including removal of the sarcoma and an adequate margin of adjacent normal tissue, is the only alternative to amputation.

3. Attempts to dissect a sarcoma away from its point of attachment will result in failure of the excision.

4. Recurrence of a sarcoma in an extremity means that local excision has failed and immediate high amputation is necessary.

5. Selected cases are reviewed to illustrate some problems often encountered when dealing with this disease.

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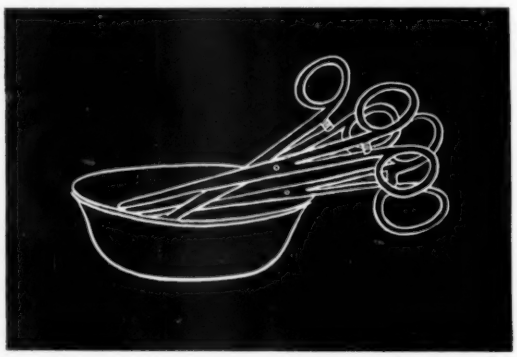

CLINICAL STUDY

Serum-Sickness Type of Penicillin Reactions

TREATED WITH SODIUM DEHYDROCHOLATE

LOUIS PELNER AND SAMUEL WALDMAN

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The serum-sickness type of penicillin reaction is becoming more frequent and more troublesome. The "occult" type, without a rash, requires differential diagnosis from many infectious diseases. Extremely gratifying results have been obtained with sodium dehydrocholate injections in the treatment of serum-sickness type of penicillin reactions.

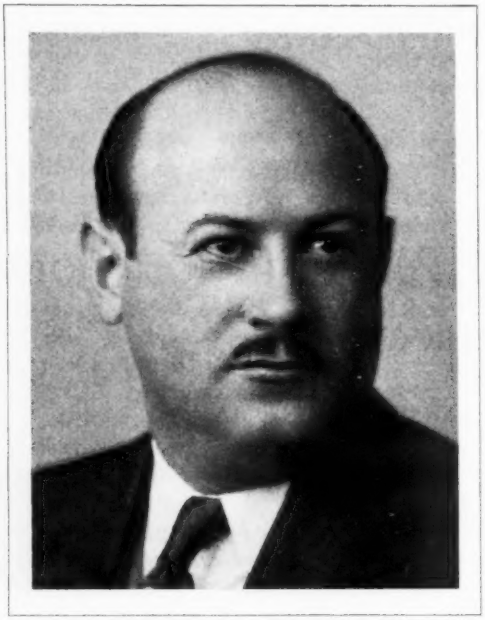
INTRODUCTION

The frequency of serum-sickness type of penicillin reactions appears to be increasing. Penicillin sensitivity is usually minor and causes only inconvenience, but occasionally the reaction is so severe as to threaten life itself. It is not our desire to record merely a few more cases of a serum-sickness type of sensitivity to penicillin; by this time every practitioner has had several troublesome cases. Brown[1] has culled 308 reports from the literature and there must be thousands of cases that go unreported.

The reports that are documented, however, show that we no longer can use penicillin indiscriminately. Every facet of a case must be scrupulously considered before an injection is given, and the possibility of harm must be weighed against the probability of bringing relief. Penicillin reactions do not necessarily cause an urticarial rash. What an anachronism it is—as happened to 2 of our patients—to treat the chills, fever, joint pains and hoarseness of a penicillin reaction with more penicillin!

ACTH and cortisone have been used effectively in the therapy of penicillin and other drug reactions.[2] It appears that their use for this condition will stand the test of time. At the time this study was undertaken, they were very difficult to procure. The possibility occurred to us that dehydrocholic acid, which has a nuclear structure similar to that of cortisone, might be effective in the treatment of penicillin reactions. In our hands, sodium dehydrocholate therapy has proved to be remarkably effective for this condition.

Unknown to us at the time this study was begun, sodium dehydrocholate had been used for urticaria more than 10 years before. Shay, Gershon-Cohen and Fels[3] used it successfully on several patients when all other methods of treatment had failed. They found that the patients in whom it was beneficial had evidences of hepatic dysfunction as shown by bromsulfalein retention. Although our reasons for using sodium dehydrocholate were different, they are not absolutely inconsistent with their views. In any event, the results were equally gratifying and therefore deserve documentation.



SAMUEL WALDMAN

LITERATURE ON PENICILLIN REACTIONS

The most exhaustive study in the literature on penicillin reactions is the article by Brown,[1] who reviewed the literature from March 1943 to October 1948 and listed 142 references. No attempt will be made to duplicate this gigantic task but, instead, some comment will be made on Brown's survey and later reports will be analyzed.

Brown's summary may well be used as our starting point: "The (penicillin) reactions occur most frequently in patients who have had several courses of penicillin. The continuation of penicillin treatment in a patient who has reacted with urticaria may or may not be tolerated. Skin tests are unreliable in predicting the occurrence of reactions and the antihistaminic drugs may or may not control the reaction and permit continuation of penicillin therapy."[1] Tuft[4] stated that all persons can be sensitized. Factors which influence sensitization are the amount and nature of the material injected, the route of administration and the interval between injections.

Sensitization is more likely to result from intravenous than from subcutaneous injection. It is also more likely to occur if there is a latent period between injections than if they are given daily. Sensitivity may also occur from local use of penicillin; therefore, some other drug should be used locally.

Reactions can occur soon after injections, sometimes within 20 to 30 minutes. Fortunately such cases are quite rare. They may be fatal, however, and are always extremely disturbing. One of the case histories in the literature reveals the following:[5] About 15 to 20 minutes after the injection of 200,000 units of crystalline sodium penicillin G in 1 cc. of sodium chloride with 0.5 cc. of 1 per cent procaine, the patient went into severe shock with extreme dyspnea, severe hyperemia and profuse sweating, rapid pulse, lowered blood pressure, agitation, choking, tightness of the chest, weakness, generalized itching and asthmatic wheezing. An intravenous injection of BENADRYL® improved the patient's condition in 10 minutes.

Waldbott's[6] patient had an almost similar story with collapse and death a few seconds after a supposed intramuscular injection. The drug may inadvertently have been given by the intravenous route.

One of our patients developed an anaphylactic response to a skin test made with crystalline potassium penicillin G, 1000 units per cubic centimeter. She had to be given ADRENALIN® several times and benadryl before recovery began. This is not the type of sensitivity about which we are concerned at present.

THE most commonly encountered reaction to penicillin simulates serum disease. It is characterized by an incubation period of from 7 to 14 days and usually consists of urticaria, angioneurotic edema, itching, fever, migratory joint pains and joint swelling. Occasionally a purpuric rash is a symptom. The reaction always occurs after a previous injection or course of penicillin.

Another type of sensitivity is the eczematoid, trichophytid-like type based on a previous sensitivity produced by a fungous infection. The so-called "spontaneously" sensitive cases belong to this group, according to Peck.[7] This form of sensitivity manifests itself by an erythematovesicular reaction which tends to localize on the

hands, feet and in the groins. It may become a generalized exfoliative dermatitis.

Among authorities there is a marked difference of opinion concerning skin tests for penicillin sensitivity. Peck[7] used an immediate intradermal skin test and a patch test, both of which he considers to be of little value. He also used a delayed cutaneous test which is read after 48 hours. A positive reaction consists of an area of erythema with edema and infiltration about 1 cm. in diameter. Peck regards the 48 hour cutaneous test as having great value in detecting penicillin sensitivity of the serum-sickness type. It is our contention that the immediate reaction denotes sensitivity of the immediate anaphylactoid type. One wonders about the value of a test that requires a 48 hour waiting period when the use of penicillin may be an emergency measure; however, such a test might be useful before penicillin is administered for treatment of syphilis.

LOUIS PELNER

DEATHS ATTRIBUTABLE TO PENICILLIN SENSITIVITY

There are several reports of deaths consequent to severe penicillin reactions of the delayed type. An early report is that of Wilensky,[8] whose patient received 30,000 units of penicillin every four hours for five days and then developed a temperature of 104° F. with the appearance of a scarlatiniform rash over the trunk, abdomen and thighs. By the sixth day the rash became more severe and spread to the chest, neck, face and arms. The patient died of "delayed anaphylactic shock" on the eighth day. Walker, Johnson and Kollnos[9] mentioned a death in which acute necrosis of the adrenal cortex was found. Presumably a functional insufficiency may be present in some cases of severe sensitivity without revealing actual necrosis.

Spain and Clark's[10] patient was given penicillin preoperatively and postoperatively for a cecostomy and developed agranulocytosis and died. Although the authors admitted that the relationship was inconclusive, they felt that the signs pointed to penicillin as the cause of death.

Rabinovitch and Snitkoff[11] reported the case of a patient who developed a severe generalized rash, fever, vomiting, pulmonary congestion and jaundice 14 days after penicillin was given following an operation for a ruptured appendix. The authors stated that the patient's clinical picture resembled that seen in severe third degree burn.

Berne's[12] patient developed a pinpoint erythematous rash which progressed to a bullous dermatitis and finally became purpuric in nature. The patient died on the fifth day.

It appears that none of the patients who died had an urticarial rash; instead the rash was scarlatiniform, bullous or purpuric.

OCCULT PENICILLIN REACTIONS

THE ultimate in absurdity would seem to be treatment of occult penicillin reactions with penicillin, yet this has occurred several times in treatment of patients described in the literature and in 2 of our patients (cases 2 and 5). Difficulty in recognizing penicillin sensitivity is especially likely to occur when the syndrome does not include cutaneous manifestations. Several additional cases of this type of penicillin sensitivity have been recorded by Corcoran.[13] One of the patients presented fever, nausea and lassitude as evidence of her penicillin sensitivity.

These symptoms cleared as soon as penicillin was discontinued. The second patient developed fever and a psychic disturbance which cleared on discontinuance of penicillin. Our patient developed fever, chills and joint pains approximately two weeks after treatment with penicillin. Since there was no urticaria, the physician thought he was dealing with a fresh respiratory infection instead of with a penicillin reaction, and gave more penicillin.

Chapin[14] described an interesting case that simulates the history of our patient. Chapin's patient had received penicillin three months and again six weeks prior to admission to the hospital. He developed a mild urticaria the day after the last injection and two weeks later developed migratory joint pains. A week after his hospital admission, several teeth were extracted under penicillin protection. The penicillin was discontinued when pruritus developed. Thereafter the patient developed joint pains, laryngeal edema, dyspnea and cyanosis. He responded to adrenalin and oxygen inhalation. It is quite likely that the joint symptoms present originally were due to penicillin sensitivity.

TREATMENT OF SERUM-SICKNESS TYPE OF PENICILLIN REACTIONS

Many forms of treatment have been used in the recorded cases of serum sickness-like penicillin sensitivity. A partial list includes all of the known antihistamines, intravenous calcium, epinephrine, ephedrine, vitamin B complex, vitamin K, DEMEROL®, intravenous niacin, intravenous glucose, intravenous procaine, autohemotherapy, ACTH and cortisone.[2,15,16] All these have been unsuccessful, except perhaps intravenous procaine, ACTH and cortisone. Procaine has often failed to relieve the patient.[16] The antihistamines appear to offer only extremely temporary benefit. According to Dreisbach,[17] the relief obtained with PYRIBENZAMINE® and benadryl in clinical reactions to penicillin is not objective, but is related to the peripheral sensory depression caused by these agents. Neither benadryl nor pyribenzamine administered subcutaneously in optimum dosage prevented the development of typical Arthus-type skin reactions in rabbits sensitized with penicillin or horse serum. Likewise, reactions were not prevented by subcutaneous injection of benadryl or pyribenzamine mixed with penicillin and horse serum. However, pyribenzamine and benadryl prevented the development of a typical histamine scratch response when these substances were mixed with it.

Zussman[18] also reported a serum-sickness type of penicillin reaction that resisted every known antihistamine.

Intravenous procaine has many adherents for the treatment of this type of penicillin sensitivity. However, it has often been proved to be ineffective and sometimes dangerous.[16] Careful supervision during administration is necessary.

Our method of treatment has much to recommend it. It has not failed so far in any patient with serum-sickness type of penicillin sensitivity.

Five cubic centimeters of sodium dehydrocholate (20 per cent solution) is given intravenously every day or every other day, depending on the severity of the penicillin sensitivity. In addition, one tablet of dehydrocholic acid (3¾ gr.) is given orally three times daily. In one of our cases, the oral method of administration was sufficient to improve the condition.

CASE REPORTS

Case 1—A. M., a 38 year old man, developed a fever ranging from 102° to 104° F. associated with a severe sore throat. He was given three intramuscular injections of procaine penicillin, 300,000 units each, on three successive days. Three days following the last injection, and six days after the initiation of penicillin, his lips began to swell. There were tender, swollen areas on his arms and legs. In addition he had marked joint pains. He was given the following medications: benadryl, pyribenzamine, HISTADYL® with ephedrine, calcium gluconate and benadryl intravenously and epinephrine subcutaneously. None of these medications caused any improvement in the patient's condition.

The patient was first seen by one of us after his penicillin reaction had been present for two weeks. By this time, in addition to his original

complaints, he had developed tightness in his throat, hoarseness, difficulty in breathing and a massive swelling of both arms and forearms. He had giant hives all over his body. He was given sodium dehydrocholate, 5 cc. intravenously daily for four days, and in addition was given one dehydrocholic acid tablet three times daily after meals. By this time he was markedly improved. One week later he noticed that he had a recurrence of dermatophytosis of both feet; this was treated with undecylenic acid ointment with improvement in several days. The penicillin reaction had not returned.

THREE months later the patient accidentally cut himself. At the hospital, preparatory to administering a tetanus antitoxin injection, a skin test was done. Because of a positive skin reaction he received no antitoxin. About 10 hours later, he had giant urticarial wheals all over his abdomen. He had pain in his throat associated with hoarseness and difficulty in breathing and there was swelling of the ears, legs, lips and cheeks. He was given sodium dehydrocholate, 5 cc. intravenously, and dehydrocholic acid tablets to be taken every four hours. The following day he felt much better. There was no shock and the hives were few in number. He was given another injection at this time. The following day he was seen again and was given another injection because he felt his joints to be slightly painful. There has been no recurrence of symptoms.

Case 2—P. P., a 44 year old man, stated that in April 1950 he developed chills, sore throat, fever and cough. This was diagnosed as a virus infection for which he received several injections of penicillin, and aspirin by mouth. Since then he had had bouts of chills, fever, hoarseness and pains in his joints at intervals of about two weeks. For each of these he had received several injections of penicillin. These attacks would subside only to recur at intervals of ten days to two weeks. He had never had any hives during these periods.

Four weeks before being seen by one of us he developed chills, sore throat, fever, dryness of the mouth and pain in his finger tips. He was given an injection of procaine penicillin, and CHLOROMYCETIN® orally. Forty-eight hours later he had massive swelling of his extremities, generalized giant hives and a temperature of 105° F. The feet and hands had swelled massively. He had difficulty in walking because of pain in both ankles. In addition, he had lost 15 pounds in the preceding three months and his appetite was poor.

The diagnosis in this case was in doubt because of the duration of his illness. Before coming to the office he had received injections of benadryl, tablets of pyribenzamine, and ephedrine and adrenalin in aqueous solution and in oil. These were given for about a week without effect.

Examination revealed massive swelling and redness of the extremities, generalized hives, a reddened throat, occasional wheezing throughout the chest, a slight systolic murmur at the apex, but no enlargement of the heart. The liver and spleen were not enlarged and, with the exception of a temperature of 102° F., there were no other pertinent findings. Because of the possibility of a subacute bacterial endocarditis, a blood culture was taken which was later reported negative. A blood count showed the following: hemoglobin 94 per cent (16.0 gm.); red blood cells 4,690,000; color index 1.0; cytology normal; white blood cells 14,100; differential study: neutrophils 69 per cent; polynuclears 68, stabs 1; large lymphocytes 2; small lymphocytes 27; eosinophils 2.

He was given an intravenous injection of sodium dehydrocholate, 5 cc. daily, as well as a dehydrocholic acid tablet three times daily, for four days. The swelling of his legs and the hives were markedly diminished. At this point, he developed severe itching between his toes, which was revealed as dermatophytosis. This was treated with undecylenic acid ointment. After four days of therapy, the hives and swelling of the extremities were gone. His appetite was better and he returned to work. The tablets were continued for three additional days, and there was no recurrence of his disability.

Case 3—P. D., a 42 year old man, had a carbuncle on the left thigh and an infected ingrown toe nail for which he was given 500,000 units of penicillin on four consecutive days. Six days after the start of penicillin therapy and

three days after the last injection was given, the patient developed generalized giant hives, swelling of the arms and legs and a fever of 102° F. Over the telephone he was instructed to take pyribenzamine and ephedrine. This proved to be without effect, so after three days the patient came to the office and was given sodium dehydrocholate, 5 cc. intravenously. This was repeated on two subsequent days. By this time all the symptoms had disappeared and he was back again at work.

Case 4—M. G., a 65 year old man, was being treated with aureomycin for upper respiratory infection and virus pneumonia. He developed a phlebitis in the varicose veins of his right lower extremity, and 600,000 units of aqueous procaine penicillin was given daily for this complication. Five days after the first injection he developed severe pain in both shoulder joints, both hip joints and the right knee joint. These joints were swollen and tender but not red. No skin rash was noted at any time. The possibility of penicillin sensitivity was strongly considered, but an acute rheumatic process could not be ruled out. The pain and tenderness in his joints did not respond to massive therapy with salicylates. Penicillin injections were stopped. Thereupon 5 cc. of sodium dehydrocholate was given intravenously for three consecutive days. After the second day the pain in the joints had diminished and after another day the pains were gone.

Case 5—J. M., a 22 year old man, developed a severe Vincent's infection of the mouth for which penicillin was administered, 300,000 units twice daily, intramuscularly, in addition to penicillin lozenges containing 5000 units each. Two weeks after the initial injection the patient developed a generalized pruritus, rash, fever and disseminated arthralgia for which his physician instituted more vigorous penicillin therapy. No relief ensued; instead, the wrists, elbows, knees and ankles became more swollen, and edema of the legs and feet appeared. Penicillin administration was continued and, since there was still no relief, aureomycin was begun orally. Antihistamines were given but failed to allay the itching or the rash. The pains increased and his hands and feet became so edematous that the fist could not be clenched and shoes could not be worn. Shoulder pain was so intense that abduction became markedly limited, resembling a "frozen" shoulder. His temperature remained elevated (101° to 103° F.) and exfoliation of the palmar and plantar skin was evident.

Four weeks after the first injection of penicillin, the patient was seen by one of us and a diagnosis of "serum-sickness type of penicillin reaction" was made. At this time the patient was unable to walk. For six consecutive days, he received 5 cc. of sodium dehydrocholate, 20 per cent solution, intravenously daily, as well as tablets of dehydrocholic acid, 3¾ gr. three times a day. Because he presented a beefy red tongue, attributable to oral use of penicillin, he was also given vitamins B complex and C intravenously.

Within 24 hours after the initiation of therapy, the joint pains began to subside and the patient could walk. Daily improvement continued until there was a complete absence of pain in six days. The edema and rash disappeared in two days. The desquamation continued until almost a complete glove and stocking mold was removed. No recurrences were noted.

Case 6—A. G., a 26 year old man, received one injection of 300,000 units of penicillin for a severe pharyngitis. The pharyngitis improved within 36 hours but the patient developed bilateral shoulder pain and his temperature rose to 100.4° F. Both hands became so edematous that the fist could not be clenched except with great difficulty. Marked itching and palmar erythema developed. Intensive antihistaminic therapy for two days gave no relief. The pruritus was intolerable. Dehydrocholic acid in 3¾ gr. tablets was given every 4 hours. Relief was apparent 24 hours later. The edema subsided; however, the skin of both palms desquamated in lamellar fashion. No recurrence was noted.

DISCUSSION

The mode of action of sodium dehydrocholate in penicillin reactions is unknown. Shay and his co-workers[3] found the treatment effective in cases of urticaria which had resisted all other methods of therapy. Since they found that some of their patients showed bromsulfalein retention as the only other objective find-

ing, they assumed that sodium dehydrocholate acted by improving liver function. These authors also found sodium dehydrocholate effective in other types of allergy such as bronchial asthma, chronic eczema, intestinal allergy and hay fever.

Shay felt that dehydrocholic acid therapy in refractory allergic states was based on the hypothesis that an abnormally functioning liver enables inadequately split protein products to reach the general circulation. Such products may pass through the intestinal mucosa in the case of oral allergens, and then enter the liver by the hepatic circulation. Owing to dysfunction of the liver cells, the split protein products are not detoxified[1] but escape into the general circulation, where they reach sensitized organs and call forth an allergic response. In the case of allergic reactions to drugs, the products would still have to be detoxified by the liver, by whatever route the drug is given.

We first began to use sodium dehydrocholate because of the similarity in its chemical structure to that of cortisone. Dehydrocholic acid is triketocholanic acid and, along with the adrenal steroids, it has the cyclopentenophenanthrene structure.[19] Dehydrocholic acid is not a natural bile acid, but is an oxidation product of desoxycholic acid. Desoxycholic acid is today the starting point for the synthesis of cortisone in vitro. Cortisone is an effective therapy for penicillin reactions, and we have found that sodium dehydrocholate is also effective. Similarity in structure is no assurance of similarity in effect, and we have no definite evidence that sodium dehydrocholate acts like cortisone. There is evidence, however, that dehydrocholic acid has at least one of the functions of the adrenocortical steroids—that of reducing increased capillary permeability.[20] Increased capillary permeability may be the basis for some allergic reactions.

Sodium dehydrocholate has been used with salutary effects in the serum-sickness type of penicillin reaction.

The sodium dehydrocholate solution (DECHOLIN SODIUM®) and dehydrocholic acid tablets (DECHOLIN®) used in this study were supplied by the Ames Company of Elkhart, Indiana.

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GENERAL PRACTICE *Review*

To provide the general practitioner, as well as the specialist, with concise, readily available information on the latest, proved methods of treatment of conditions commonly encountered in an average practice, POSTGRADUATE MEDICINE *offers this department to its readers. It is not, of course, intended to present these discussions as the only acceptable therapeutic procedures to be used, but rather to offer simple regimens and recommendations based on the extensive experience of the physicians who prepared these summaries.*

Treatment of Acute Mastoiditis

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BALLENGER

ACUTE mastoiditis is almost always secondary to a middle ear suppuration. The primary form is almost never seen and, if it did occur, the infection would probably be transmitted by the blood stream. The surgical stage of acute mastoiditis is rarely encountered at the present time because of modern therapy with the sulfonamides and/or the antibiotics, and secondly, because a seemingly less virulent type of hemolytic streptococcic infection prevails. In recent years the beta type of the hemolytic streptococci has been recovered from the mastoid cavity in over 90 per cent of all cases.

The symptoms of acute mastoiditis are those of an acute suppurative otitis media, but in an exaggerated form: i.e., the temperature is higher, the toxemia greater, the discharge more profuse and persistent, the cell count higher, and the pain—if present in an acute otitis—is increased and continues much longer. In addition to pain, tenderness upon pressure over the mastoid antrum posterior to the auricle is present early in almost all cases, and usually persists until adequate drainage has been established. Tenderness to pressure over the tip of the mastoid process is frequently present as well. Usually the entire mastoid area is more or less sensitive. The skin over the mastoid process frequently becomes infiltrated, sometimes producing redness and swelling. Palpation with the finger over this region gives the sensation of the soft tissues being slightly thicker or having a "velvety" feel when compared to the normal side. If a pus collection has formed beneath the periosteum, because of a perforation of the mastoid cortex, the auricle will stand forward and in extreme instances almost approach a right angle to the side of the head.

As a rule the discharge in acute mastoiditis is quite profuse, has a darker, grayer appearance, and is more frequently tinged with blood than is the pus in an uncomplicated acute suppurative otitis media. When the secretion is wiped or mopped off the tympanic membrane, it has a tendency to reappear quickly. The secretion usually pulsates with the heart beat, a characteristic feature of acute mastoiditis. In a later stage—that is, after about three weeks—when

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some of the mastoid bony structure has decalcified, inspection of the auditory canal may reveal a sagging or narrowing of the postero-superior canal wall. This is due to edema in some instances, but usually to a partial breaking-down of this portion of the canal wall. If caused by the latter, the simple mastoid operation is normally indicated. In many cases this sagging is absent, even though a destructive mastoiditis is present.

The perforation of the ear drum is usually central and not large at first, but in the later stages may enlarge, even extending to the margin of the ear drum in a few virulent infections. Granulations may form and be observed protruding through the perforation after from three to six weeks of suppuration. The granulations tend to block the drainage through the perforation and as a result prolong the mastoiditis.

The white cell count in uncomplicated mastoiditis may vary from 12,000 to 20,000. If much higher, additional septic processes elsewhere in the body should be suspected. The hemoglobin and red cells are not affected as a rule. If a rapid fall in the number of red cells and the hemoglobin is found, complications involving the blood, such as a lateral sinus thrombosis, should be suspected.

In many cases the roentgenogram of the mastoid will show presence or absence of a mastoiditis and after two or three weeks will indicate whether a partial or complete decalcification has taken place. However, the roentgenogram rarely denotes the severity of the infection.

Acute mastoiditis should be differentiated from a severe diffuse type of furunculosis of the external auditory canal in which a marked inflammatory swelling of the canal wall and postauricular region is present with a more or less purulent discharge. Direct pressure over the mastoid away from the auricle would not produce tenderness in furunculosis, but manipulation of the auricle would be painful. In both conditions pus would be present in the canal, but would be much more profuse from mastoiditis. The ear drum, if seen with furunculosis, would be intact. The toxemia and temperature, if present with furunculosis, would be less than with mastoiditis. Early roentgenograms of the mastoid area may show cloudiness in furunculosis because of the soft-tissue swelling, but cell destruction would be absent. In addition to furunculosis, the pain of acute mastoiditis should be differentiated from an inflamed postauricular lymph node and the various neuralgias located in the ear and mastoid region.

SPECIFIC TREATMENT

Treatment in the early acute phase of mastoiditis consists of an adequate dosage of one of the sulfonamides and/or one of the antibiotics given over a sufficiently long period of time to maintain in the blood a constant high level of the agent used. The high blood level should be maintained throughout the acute phase. Penicillin would be the agent of choice if the infection were due to the hemolytic streptococci. Sulfadiazine in adequate dosage with a high fluid intake is also satisfactory.

As practically all cases of acute mastoiditis are secondary to an acute suppurative otitis media, the ear drum has already ruptured or has been incised. If drainage through the ear drum seems to be blocked, or is not adequate, an enlargement of the incision or rupture should be done with a sharp bayonet-shaped paracentesis knife. The rapidly forming discharge should be mopped out daily by the physician, or the ear may be irrigated by the nurse or mother twice daily with a warm saturated solution of boric acid. After the removal of the secretion by mopping or irrigation, five or six drops of equal parts of alcohol and saturated solution of boric acid should be instilled in the canal and left to evaporate. In many instances a light dusting with powdered sulfadiazine into the auditory canal and over the ear drum will be beneficial.

Dull, throbbing pain in the middle ear and mastoid cavity is relieved to a great extent by some form of hot applications. The most efficient means of using heat is the hot wet boric acid pack. Strips of gauze or some similar cloth, soaked in the hot solution, are placed behind the auricle over the mastoid process and in front of the auricle over the auditory meatus. The gauze may be covered with a thin sheet of rubber or oiled silk and then with a layer of flannel. This retains moisture and heat. Packs should be renewed about every two hours for several days or until relief is obtained.

INDICATIONS FOR SURGERY

If the pain and temperature persist for three or four weeks with some toxemia present and without diminution in the discharge, the simple mastoid operation should be considered. The operation should also be considered if the otorrhea has continued from four to six weeks even though pain and temperature are slight or absent. The discharge, if permitted to run for several weeks, may result in a chronic suppurative otitis media with some permanent loss of hearing in the affected ear.

Sagging or bulging of the post-superior canal wall, continued infiltration, and tenderness over the mastoid process, or the presence of a subperiosteal abscess over the mastoid cortex would be an additional indication for the simple mastoid operation.

Beginning meningeal irritation or positive blood cultures suggesting a thrombosis of the lateral sinus which is not responding to the sulfonamides or the antibiotics would constitute positive indications for the mastoid operation.

The simple mastoid operation, when indicated and properly done, should result in a dry ear, an intact ear drum, and normal hearing. Fortunately with today's modern therapy, the mastoid operation for acute mastoiditis is seldom necessary.

Management of Abortion

GEORGE E. JUDD*

LOS ANGELES

JUDD

One of the neglected subjects in medical education and in obstetric textbooks is that of abortion. When we realize that 1 out of every 3 or 4 pregnancies terminates in abortion and compare that incidence with the relatively few pages in the average text devoted to that subject, the neglect begins to take on significance.

This neglect would be excusable if we were not confronted with reports that abortion was the cause of 27 per cent of maternal mortality[1] and perhaps a large part of the maternal morbidity as well.

Abortion is concerned with the first 16 weeks of a pregnancy. It is commonly classified in four different ways: (1) on the basis of etiology as criminal, spontaneous, or therapeutic; (2) on the basis of stage of development at the time of the abortion as threatened, inevitable, incomplete, complete, or missed; (3) on the basis of recurrence as habitual; (4) on the basis of complication as infected.

The scope of this discussion does not permit the subject of criminal abortion to be given more than wholehearted condemnation for its presence in our society. Though it forms the etiology of much of our female disability and sterility, we can only estimate or guess at its frequency. The answer to this problem will, I am afraid, be long in coming.

The present discourse will be concerned with the way we have managed the problem of spontaneous abortion in our practice. We recognize many areas of controversy in methods of handling various phases of the problem. The methods discussed here are not offered as the only ways to manage the problem, but rather as offering the management I have found to give

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best results. We will discuss threatened, incomplete, complete, missed and habitual abortion.

THREATENED ABORTION

Whenever a patient with an early pregnancy begins to bleed vaginally, that pregnancy is threatened. To be sure, in the vast majority of the cases, no pregnancy test has previously been done. The presumptive signs of pregnancy are as a rule the only ones available. Delay of menstrual period, nausea and vomiting, tender and occasionally enlarged breasts, bladder irritability, and a sense of fatigue usually are present in some combination. These do not prove the presence of a pregnancy but are only indications of its probable presence. Depending upon available facilities, the delay between suspicion and proof may extend from hours to days.

If possible, whenever delay of the period has occurred, the establishment of a diagnosis of pregnancy is most helpful to eliminate the treatment of uterine bleeding from nonpregnant conditions. In most cases, this bleeding is reported by telephone and decision as to first treatment must be made at that time: (1) Prescribe bed rest without bathroom privileges as the first most important item. (2) Tell the patient to save all tissue passed and keep it in water for subsequent examination. Reassurance at this time is essential. This can be facilitated by explaining the plans usually followed in these cases. Without going into a lengthy and complicated discussion about abortions in general, one can easily say, "This bleeding, if slight, may be only a threat to the pregnancy and not necessarily its termination. We are inclined to let the next few hours decide how serious this threat may be. Put your wife in bed without elevation of either head or foot of the bed. I have never seen any benefits from changes in the usual position of the bed. Save any tissue that passes so that we may examine it. Do this by putting it into a small jar and covering it with water so it will not dry out. If the bleeding reaches the proportion of the flow usually encountered at the menstrual period or heavier, we will have her brought into the hospital. If there are mild cramps, use aspirin, ANACIN® or EMPIRIN®. If the cramps are severe, hospitalization will be necessary."

The use of estrogens and/or some progesterone preparation may be instituted at this time. If bleeding is the only symptom, and I am certain a pregnancy is present, I usually prescribe 25 mg. of stilbestrol by mouth and repeat it hourly until bleeding stops, usually stopping at three to four doses. More has been given without untoward effect. Indiscriminate use of stilbestrol without being certain of the pregnancy only complicates a confused picture. If cramps are present, progesterone by sublingual route or hypodermically is given. Remember that it takes twice the dosage by mouth to equal the dosage by hypodermic. Here also large doses have been used without untoward effect. It is well to keep a sense of economic balance and remember that large doses of progesterone can be a real financial load to the patient. Do not waste a good product or a patient's resources needlessly. If the bleeding stops, I continue the stilbestrol on a gradually increasing schedule as outlined by Smith and Smith,[2] increasing 5 mg. daily every two weeks until the sixteenth week, and 5 mg. daily every week thereafter until the thirty-fourth to thirty-sixth week.

Progesterone has been used by many with very good results. However, I have reserved it for the patient with painful uterine contractions.

When we realistically judge our salvage rate we are struck by how little we affect the course of these pregnancies. The issue so often is already decided before treatment begins.

If the bleeding and cramps subside, I cautiously allow the patient first to go to the bathroom and then to remain out of bed for brief intervals, returning to bed at the first sign of recurrence of either cramps or bleeding. Here knowledge of each individual patient is important in gauging return to activity.

INEVITABLE ABORTION

Threatened abortion can change to inevitable or incomplete abortion. Rough standards of judgment are as follows: (1) a degree of bleeding comparable with the usual menstrual flow, (2) cramps too severe to be alleviated by use of the usual household remedies, (3) passing of chorionic or decidual tissue, (4) an open cervix, and (5) rupture of the amniotic sac. Patients exhibiting the first two symptoms may con-

ceivably continue pregnancies, but their chances are better in the hospital. The last three conditions definitely point to inevitable abortion. The rupture of the amniotic sac must be cautiously and carefully determined, as reports by the patient of escape of fluid from the vagina may be in error. Once hospitalized, the patient may still be watched until you are sure the pregnancy is irretrievably lost.

The loss of chorionic or decidual tissue, the open cervix, or bleeding of exaggerated proportions are the usual indications to take the patient to surgery and, under gas or PENTOTHAL SODIUM® anesthesia, make certain that the uterine cavity is free from retained secundines. The so-called sponge forceps' removal of tissue may involve more than the use of sponge forceps. Occasionally the dull curette, and in several instances a sharp curette, has been gently used where I have felt tissue adherent to the uterine wall. There must be great care in the use of the sharp curette. It is imperative that all intrauterine instrumentation be gentle especially when carried on in the presence of a gravid uterus. At times finger curettage may be safer, especially if the pregnancy is beyond the fourteenth week, or if much tissue is adherent.

After the uterine cavity is satisfactorily freed from retained secundines, the cavity is then packed with dry gauze, and sprinkled well with sulfanilamide crystals. This packing is removed in eight hours.

The obvious question, "Why do anything in the way of intrauterine instrumentation?" is answered by the item of time. Curettage and packing are definitely indicated in the patient who is bleeding severely, whereas in the very early pregnancy, five to seven weeks, where the chorionic mass may be easily and apparently completely passed, we can be more conservative. The group in between are the abortion patients who often appear to have passed all the tissue and are bleeding very little, only to suddenly flow profusely or more often continue to bleed over a long period. Small amounts of retained tissue can persist and be the cause of bleeding for months. To insure the patient a speedy and usually controlled end to her problem, we have found sponge forceps' removal of the retained tissue gives us the best results.

TREATMENT OF EMOTIONAL REACTIONS

The emotional side of the treatment is very important. Most of these patients are depressed by the "loss of the baby." They visualize the end product of any pregnancy as a baby, and begin to do so as soon as they get pregnant. They are fearful many times that the abortion implies no more children, and especially that it is the result of some personal or medical neglect in the past or the present. Too often, without justification, we are charged with the loss of a pregnancy because of a vaginal examination. Many times patients' guilt feelings are given tangible foundation by the abortion.

A simple explanation may be offered: (1) that one abortion occurs out of every three to five pregnancies; (2) that a high percentage, 50 per cent or more, of these lost pregnancies had no fetus present and would never have terminated in a baby; (3) that the occurrence of one or perhaps a second spontaneous abortion does not signify that future pregnancies and children will be difficult to achieve; and, (4) that within three to six months, depending on a careful analysis of conditions, a new pregnancy can be undertaken. It is well to keep in mind that lasting damage can come from ill-advised and inaccurate statements. Tell only what you are sure of, never speculate as to etiology. It is no reflection on us to say, "I don't know," to some of the many questions that are asked of us by the patient, her husband or the family. This usually suffices to allay fears and gives the reassurance needed to carry them over their disappointment.

HABITUAL ABORTION

Whenever two or more spontaneous abortions occur, the problem of habitual abortion is presented. Much has been written concerning treatment of this condition. The lengths to which some treatment programs go are beyond the economic ability of the average patient. It is well to recognize that there may be some difficulty in the reproductive physiology of the family, not necessarily in that of the wife or husband alone.

Salient points to keep in mind—Remember that to consider the wife only, in terms of fail-

ure, is illogical. (2) It is well to reflect that we vary from day to day in all our bodily functions and that single isolated tests of tubal patency, endometrial biopsies, morning temperature curve and sperm analysis may not give the true picture for a particular patient. I have found many changes by repeating these tests at different times. (3) Don't be too hasty in giving a bad prognosis. We all see patients who have been told they would never get pregnant or would never be able to carry a pregnancy to term, produce large families. (4) Promotion of general body well being and mental relaxation is an important item. (5) Each case must be individualized, for a fixed routine conscientiously followed may miss the boat.

The details of sperm examination have been well outlined in the various tests and in the literature and need not be discussed here. It is my practice to refer these husbands to a urologist who is interested in the subject of male sterility and low fertility.

The study of the female reproductive physiology has also been well outlined in the literature and texts. The study of ovulatory activity can be done by means of the endometrial biopsy and temperature curve. Mechanical problems of stenosis of tube or cervix usually are encountered in failure to conceive, not in habitual abortion. Occasionally fibroids or laceration of the cervix may be the cause of habitual abortion. It is well to note that the man who pays the most attention to details has the best batting average of successful results, but that even the most careful fail too many times.

MISSED ABORTION

Fortunately, the missed abortion, i.e., the failure of the uterus to empty its contents after the fetus dies or fails to develop, is a rare complication of pregnancy.

This condition often is indicated by what appears to be a threatened abortion without the loss of chorionic tissue, or there may be no bleeding at all. The important item is that the uterus fails to develop. Suspicion of this condition occurs when the fundus shows no growth or an actual reduction in size. However, a frank dogmatic diagnosis may be difficult or even unwise. First, the problem of a formal declaration of fetal loss is not always accurate, and second, the time lag between suspicion and the passage of tissue may be as much as several weeks. During this time, the patient must maintain some semblance of mental composure in spite of the thought that the "pregnancy is dead," and all her mental aversion to the retaining of the dead products of conception. Her attitude will in no way be helped by well meaning friends and relatives who can always conjure up a story, real or fancied, about what happened to a friend, etc., etc. I know of few problems in medicine where more skill is required in handling the patient. I feel it is important to voice the suspicion of fetal death with the qualifying statement that we have been wrong before on various occasions. The greatest danger is impetuosity. Panic has forced the unnecessary invading of the uterine cavity with a resulting high incidence of infection and complication, and the occasional interruption of a normal pregnancy.

It is well to warn the patient against the general broadcasting of her doctor's suspicions to friends and relatives, and to explain that the panic she may feel can be increased by the thoughtless and untimely anxiety-producing talk that almost surely will follow.

I know also of no other instance where sharing the responsibility with a colleague can be more helpful to the mental welfare of the patient. The treatment is watchful waiting until the physiology of the uterus eliminates the remaining products of conception. Occasionally, if bleeding is heavy, a gentle uterine curettage will be all that is necessary. I believe we are all impressed by the ease with which these problems so often are handled by the normal physiology of the patient.

Here again reassurance as to the personal significance of this occurrence is an essential part of the treatment program. There is no justification for discouragement of future pregnancies, nor is the misfortune due to any acts of commission or omission by the patient. Most of the time it happens without known causes.

Space does not permit a discussion of therapeutic abortion with its many aspects of indication, procedure and the important decision

of when the pregnancy should be interrupted from below and when from above. For the same reason, the treatment of infected abortion introduces a big subject that obviously requires much space to touch on only the high spots.

It is encouraging to know that greater understanding of many phases of abortion is being carried forward. The studies of hormonal levels in blood and urine have pointed out some changes that are important in pregnancy, but as yet they have not reached the accuracy that is necessary to give substantial prognosis to patients. Too many pregnancies go on with a low level of blood chorionic gonadotropin or urine pregnanediol, and too many are lost with levels that seem satisfactory. Hormonal determinations of blood and urine at present are not practical for routine use and should be reserved for research. The use of the vaginal smear has not yet reached the wide use it deserves in helping to decide the difference between threatened and inevitable abortion. Many days of bed rest and hospital confinement can be saved by this procedure.

The foregoing is an attempt to set down in order some of the essentials in the treatment of various phases of this subject. Apology is made for some dogmatism which is used for emphasis and for the lack of space that prevents excursions into the interesting bypaths that present themselves from time to time. The areas of disagreement and difference of procedure that come to mind must be settled by each individual doctor with each individual patient and her needs. Flexibility of thinking is especially important in the treatment of this condition.

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Antepartum Care

BERNARD J. HANLEY*

LOS ANGELES

At one time, prenatal care consisted of only two visits—first, when the physician diagnosed the pregnancy, and second, when he was called to attend his frightened patient in the mortal and agonal throes of parturition. Those days have passed into well deserved oblivion, and their passing has brought about a change so profound that one need only glance at the maternal mortality tables to realize its momentous character.

HANLEY

The candidate for parturition must be brought up to this phase of gestation in a maximum state of physical and mental preparedness. Nowhere else in the field of medicine does the physician have the opportunity to accomplish this as in obstetrics, and nowhere else is attention to details more conducive to success.

PHYSICAL EXAMINATION AND LABORATORY STUDIES

The first visit to the obstetrician should comprise a detailed history, physical examination and indicated laboratory studies. A duplicate of all the information obtained should be available at the hospital when the patient com-

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mences labor. Also at the first visit the patient is instructed to consult her dentist if she has not done so within the past three months.

The minimum laboratory work consists of a red blood cell count, hemoglobin, serology, Rh factor and a roentgenogram of the chest. The husbands should be typed for the Rh factor in cases of multigravidas who are found to be Rh negative and also in cases of primigravidas from whom a history of previous blood transfusion is obtained. If the husband is Rh positive, blood titers are started on the mother's serum at the thirty-fourth week of gestation. When blocking antibodies and agglutinins are present, titers are repeated at 10 day intervals and arrangements are made to transfuse the newborn infant at the time of delivery. In those gravid patients whose serum titers are found to be rising rapidly, induction of labor must be seriously considered. However, bear it well in mind that an infant who dies because of prematurity is just as dead as one who dies because of erythroblastosis. Furthermore, combine prematurity with erythroblastosis and the hazard to the infant is increased tenfold.

In estimating the date of confinement, it is well to emphasize to the patient that this date is merely an approximation based on the dates of her last catamenia and is not to be taken too seriously. At the same time the physician should satisfy himself that the size of the uterine corpus is consistent with the stated period of amenorrhea. If any question exists, a biologic test for pregnancy should be suggested.

As a matter of policy, a pelvic examination is indicated to determine uterine size whenever the fetal heart tones cannot be auscultated after the sixteenth to eighteenth week of gestation. By this simple technic, missed abortions are diagnosed early. A rapidly growing uterus often makes multiple pregnancy or polyhydramnios suspect and a flat plate of the abdomen should be made.

Speculum examinations are essential for all patients with vaginal bleeding during the early trimesters of pregnancy. Often a physician orders absolute bed rest for his patient without giving her the benefit of this simple procedure, only to discover later that the source of the bleeding was a circumostial erosion or a cervical polyp. Intercourse and douches are interdicted in cases of vaginal bleeding and after the thirty-sixth week of gestation.

PELVIC MEASUREMENTS

As recently stated by Eastman and Greenhill, it is now becoming apparent that external pelvic mensuration, as taught, is obsolescent and only serves to create a false sense of security. I have come to rely almost exclusively on the method of direct pelvimetry devised by McDermott several years ago. This measurement is called the "anterior pelvic depth" and its knowledge, easily obtained, permits the prognostication of the course of labor in the midpelvis and at the outlet with a high degree of accuracy. The inlet of the pelvis, of course, is measured by the diagonal conjugate.

DIET

Emphasis is placed on a high protein diet consisting of a daily minimum of one egg, one-half pound of lean meat and one quart of milk. If the patient is unable to drink milk, additional calcium is substituted. The patient is encouraged to partake of average amounts of fresh fruit, vegetables and liquids. Supplementary vitamins, iron and calcium are prescribed. If necessary, mild laxatives are ordered. Although gain in weight of the mother is unrelated to the size of the baby except in diabetics, she should be cautioned against a gain of more than 20 pounds.

CLOTHING

Well fitting garments are advisable, with support rather than constriction as the desired aim. A brassiere should be worn. The patient should be encouraged to plan to nurse her infant and a program of effleurage and massage of the breasts and nipples outlined. An elastic girdle gives excellent support to patients with flaccid abdominal musculature and often serves to alleviate tiresome and troublesome backaches. Low-heeled shoes with strong arch supports should be substituted for the other fashions of the day.

TRAVEL AND EMPLOYMENT

Profiting from unavoidable wartime experiences, permission to travel is now given less reluctantly. The patient should be warned to avoid the more hazardous modes of travel and isolated places where help is not easily obtainable. Continued employment in industry during pregnancy poses a new problem affecting not only obstetrics but the economic and social structures as well. Let common sense and practicality be the rule. Women may engage in sedentary work up to and sometimes including the last trimester.

SUBSEQUENT VISITS

As the pregnancy progresses, the patient should be seen at monthly intervals and encouraged to lead her normal life. If complications arise, she should be seen more frequently as the case may dictate. Development of the pregnancy is recorded by measurement of the height of the fundus, auscultation of the fetal heart tones, careful check of the weight, blood pressure, and urinalysis. Impending signs and symptoms of toxemia should be carefully evaluated.

COMPLICATIONS

Nausea and emesis of early gravidity still remain an obstetric enigma. However, DIMENHYDRINATE® given before meals has been fairly successful in their control. Frequent feedings and sedation have universal appeal. Sialorrhea or ptyalism of pregnancy may sometimes be controlled by giving small doses of methantheline bromide. Pyrosis or heartburn responds temporarily to the various aluminum gels.

Varicosities of the lower extremities improve symptomatically when elastic stockings are worn. However, if deemed necessary, high ligation may be resorted to at any time without hazard to the pregnancy. The pain that so frequently accompanies varices of the vulva may be satisfactorily managed by use of the familiar athletic supporter containing foam rubber cushions in the cup. Cramps or so-called charley-horses of the calf muscles are alleviated by administration of fractional doses of calcium carbonate or lime water.

The vaginitides in pregnancy are usually of the mixed type. This distressing condition is best controlled by frequent mild acid douches, attention to hygiene and the local application of 2 per cent aqueous gentian violet.

External versions to convert breech presentations are not done. I feel that it is an unsatisfactory procedure and it presents a definite risk to the mother and infant. A breech that can be turned easily can also be delivered easily as a breech, thereby increasing your experience. A frank breech in the primigravida usually cannot be converted and such cases present the real problems, so the incidence of difficult breech deliveries is not lessened. Learn to deliver a breech presentation.

Beginning with the thirty-sixth week of gestation, the patient is seen once a week and a pelvic examination is done with a clean glove without additional preparation. This is an essential part of my examination. I have done this over the years in order to evaluate the cervix and I have never had reason to change my procedure. The knowledge that is gained from this examination is of inestimable value in the management of parturition.

INDUCTION OF LABOR

My final topic concerns the elective induction of labor at or near term by amniotomy. How often are we called upon to use our best judgment and exercise our greatest skill when our physical resources are at their lowest ebb! Only by the proper evaluation of the favorable cervix can one electively induce labor with success. Unless the physician has more than a casual knowledge of the patient's cervix—and this can only be attained by repeated pelvic examinations—the elective induction of labor can be hazardous.

Pediatrics

IN GENERAL PRACTICE

For general practitioners, in whose practice is included a major proportion of the medical management of infants and children, and for the specializing pediatrician as well, POSTGRADUATE MEDICINE *presents this special regular department devoted to brief discussions by recognized authorities on their preferred methods of the treatment and management of diseases and problems of infancy and childhood.*

Speech Disorders in Children

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BROWN

COMPETENT surveys of speech disorders among school children have shown that about 5 per cent of all children present clinically significant speech problems. Although a number of different types of disorders are represented in the total, there are three conditions which are of prime importance to the physician whose practice includes the care of many children.

The first of these problems, that of retarded speech development, is of chief importance in the preschool years. The major significance of this condition lies in the variety of etiologic factors and the consequent need for careful differential diagnosis.

The child is presented by his parents with the complaint that he is "slow in talking," that he "doesn't talk at all," or with some other reference to delayed acquisition or meager use of speech. In evaluating these complaints one must get a careful history of the ages of the first consistent use of single words and the first use of combinations of two or more words. The average infant of 12 months has two or three words. These are not perfectly articulated, of course, but they are phonetic combinations which the child uses regularly to refer to certain persons, objects or actions. The vocabulary steadily and rapidly increases during the second year of life, and by 24 months the average infant is using various combinations of two or more words.

As with any other aspect of human development, a certain amount of variation is to be expected. Too often, however, the concept of normal variation is strained too far and parents are reassured and given a false sense of security when an abnormal retardation actually exists. A delay of 18 months in the acquisition of single words or of multi-word combinations is the extreme permissible limit, but we will make fewer errors if a delay of 12 months is regarded as indication for study.

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MENTAL RETARDATION

The most common cause of speech retardation is mental retardation. Every child who is being studied because of slow speech development should be referred for competent psychometric evaluation. The difficulties in obtaining a valid test of the intelligence of a young child are great, and they are much greater when the child has little or no speech. Hence, the interpretation of the results of the test must be cautious and preferably should be done by the physician and the psychologist in conference. If the test confirms the physician's impression of serious mental retardation, and if no other important cause is uncovered, the child is properly regarded as being primarily a problem in mental rather than speech development.

AUDITORY IMPAIRMENT

The next most common cause of speech retardation is auditory impairment. Every patient who seems at all capable of cooperating should have a hearing evaluation, preferably by means of an audiometer and other electronic equipment. With sufficient patience an experienced tester can obtain a great deal of information about the hearing of a preschool child. The importance of a hearing test is underscored by the fact that the parents of most 24 to 30 month old children with serious or total hearing losses complain of the child's failure to talk and are unaware of his deafness. The common statement of parents, "He hears well enough when he wants to," is practically pathognomonic of serious hearing impairment in the child. When such a hearing loss is found, the child's psychologic test may need to be re-evaluated. The proper measures for dealing with reversible losses must be instituted. Specialized speech therapy is needed, and the child's entire education may have to be in a special school.

PSYCHOLOGIC OR ENVIRONMENTAL FACTORS

Some children with normal hearing and intelligence show strikingly delayed speech development because of psychologic or environmental factors which may be analyzed into two chief elements. The first is lack of speech stimulation. Busy and preoccupied parents may not realize how little they talk to their child. Passively watching a television screen offers little stimulation to speech development compared with family conversations which regularly include the child.

Improper or inadequate motivation for learning of speech is the other main environmental factor. It is usually an oversimplification to say that the child does not need to talk because his wants are anticipated. A more accurate analysis will generally show that the child is being rewarded indiscriminately in a way that makes the rewards ineffectual as a motivation for learning. In these cases there is usually a behavior or discipline problem on the same basis as the delay in speech, and sound therapy must include rather complete overhauling of the parents' system of rewards and punishments.

FUNCTIONAL DEFECTS

Functional defects of articulation make up about 70 per cent of all speech problems in children, and are referred to by the term dyslalia. We may define dyslalia as defective articulation not associated with mental retardation, hearing impairment or significant abnormality of the organs of speech (tongue, lips, teeth, palate) or their innervation. The disorder may be characterized by mild distortion of a single sound and may scarcely justify treatment, or the speech may be almost totally unintelligible.

It is important not to attach importance to minor deviations in the speech structures. An allegedly high palate is often blamed for many defects entirely unrelated to any effect it might have. "Tongue-tie"—a short lingual frenulum—is rarely significant. Clipping the frenulum is to be condemned, whether it is done as prophylaxis in infancy or as treatment in an older patient. Certainly more patients have been harmed than helped by this procedure.

The diagnostic considerations in dyslalia are implied by its definition—psychologic examination or other clear proof of at least normal intelligence, hearing test and examination of the organs of speech. Appropriate speech therapy includes several stages: (1) ear training, so that the child learns to recognize his error and the

correct production of the sound; (2) learning the correct production, usually by trial and error under supervision; (3) habituation of the correct mode of articulation. With skillful therapy the prognosis is excellent, though severe cases usually require several years. Little reliance can be placed on spontaneous improvement, since careful study[5] has demonstrated that without therapy there is only slight change in articulatory defects after 8 years of age.

STUTTERING

The third speech defect to be considered—stuttering—has been the subject of more research than any other speech disorder. The many and complex aspects of stuttering in the older child and the adult cannot be described here. In the young child, especially in the preschool years, the problem yields readily to proper analysis and advice, and this fact makes stuttering of great importance to the physician. The incidence of stuttering is about 0.6 per cent of the total population, or about a million cases in the United States. Nearly all of these cases could have been prevented by skillful handling of the problem in its early stages.

A series of careful researches[4] has shown that repetition of sounds, words and phrases is a normal part of the speech of every preschool child. The average amount of these repetitions is 45 times per thousand words spoken. There is much variation, of course, from one child to another and also in the same child from one situation to the next. Long cycles also exist in the amount of repetition found in most children's speech. This repetitiveness is so familiar that most persons actually are unaware of its presence.

Occasionally, however, someone decides that a given child's repetitions are abnormal. They become concerned because they think the child is stuttering. It is usually a parent who first makes this diagnosis of stuttering, thus confusing normal preschool repetition with the strained, tense efforts of the adult stutterer. But the paradox is that it is precisely this misdiagnosis which eventually results in the development of confirmed stuttering. This fact has led Johnson[3] to refer to stuttering as a "diagnosogenic" disorder. It is important to note that stuttering is unique in that it is always (perhaps to be safe one should say "almost always") first diagnosed by a non-expert, whether it be a parent, a teacher or some other person unversed in speech pathology.

The thought that the child is beginning to show signs of what might become a serious problem naturally causes the parents a good deal of concern. Before long they usually start to try to help the child, telling him to speak more slowly, to take a breath before speaking or to think of what he wants to say. These homemade remedies serve only to arouse anxiety in the child about the normal and inevitable repetitions and he tries to talk as fluently as possible to gain his parents' approval. The child's natural reaction is to use force and to strain to try to say words without any non-fluency. The result of this effort is only to increase the length of the moments of non-fluency and to change their character from the original normal, easy repetition to tense blocks, often accompanied by facial grimaces.

If the parents do not react overtly but continue to be worried by the presence of repetition in their child's speech, the development of tension in the child is much slower but is none the less certain. The parental concern cannot be forever concealed from the child, and is communicated to him in various more or less subtle ways. The attempts to help result in fairly rapid onset of speech tensions in the child, often within a few months. Some unfortunate children are punished for their non-fluencies and may show tensions within a matter of days.

In cases where the child has developed little or no tension during his non-fluencies, the treatment[1] is simple, at least in principle. It consists of explaining in great detail to the parents that the non-fluencies which have been causing them such concern are actually a normal feature of the speech of young children. They must be thoroughly convinced of the essential normality of the repetition; this can be done by citing the research previously mentioned and by giving them assignments to observe closely the speech of other children whom they regard as normal. They are not told to "ignore" the repetitions nor are they assured that "if they pay no

attention to it, the child will soon stop." Rather, they are urged to evaluate the repetitions properly, and it is explicitly pointed out that the repetitions, being normal, are going to continue for a long time. This therapy is adequate only when significant speech tensions and concern relating thereto are not found in the child. In those cases which are seen early enough, the results are highly gratifying.

Since competent speech therapists are all too few, most patients with speech defects must depend on advice from clinicians whose training is not primarily in speech pathology. It is hoped that the facts presented here will enable many physicians to give helpful counsel.

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Management of Anemia in Childhood

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PIERCE

The causes of anemia in childhood are multiple and differ from those of adult life in many respects: Maternal and fetal relationships affect the factors concerned with blood formation and destruction; the rate of growth in infancy and early childhood places a high requirement on the building stones for hemoglobin synthesis; the repeated infections of childhood interfere with the utilization of iron, vitamins and foods necessary for blood cell formation, and the hereditary factors which determine the severe constitutional anemias may result in an illness which does not permit survival into adult life. Perhaps the simplest way to discuss the management of the anemias in childhood is to consider the various anemias which are common to children of different age groups.

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ANEMIA IN THE NEWBORN

Hemolytic disease of the newborn (erythroblastosis fetalis) is the most common cause of an anemia which develops in the first few hours or days of life. The sensitization of the mother may be produced by an incompatibility of maternal and fetal blood types of either the ABO or Rh systems. When the maternal antibodies enter the infant's circulation, a hemolytic anemia results from destruction of the infant's red blood cells. The Rh antibodies are more damaging than the AB antibodies and cause a more severe degree of anemia. Kernicterus, with its sequela of brain damage, is more commonly the result of the Rh incompatibility.

The mechanism of kernicterus is not understood clearly, but it is known that it is more apt to occur in babies who develop an intense jaundice within the first few hours of life, and the pathologic findings suggest a correlation with a severe degree of hepatic damage. The clinical signs of kernicterus may precede those of a severe anemia, and may in fact be present at birth. The mortality rate of this disease has been lessened appreciably by controlling the anemia with small multiple transfusions but,

in spite of transfusion therapy, the incidence of kernicterus is still high in severely affected babies. Primarily to reduce the incidence of kernicterus, the replacement type of transfusion has been employed, and evidence has been obtained that both the mortality rates and the incidence of kernicterus have been lowered by a regimen which combines (1) early treatment and (2) replacement transfusions.

The treatment of this disease actually begins by anticipating the necessity for immediate care of the infant after delivery. All babies of Rh negative women who show an increasing titer of Rh antibodies throughout pregnancy or who previously have had an affected child must be examined in the delivery room for clinical or hematologic evidence of the disease and a decision must be reached regarding the treatment.

The indications for the replacement transfusions are: (1) signs of pallor, enlargement of the liver and spleen, hemorrhagic manifestations or edema; (2) hemoglobin of 13 gm. or less in the cord blood of an Rh positive baby of a sensitized Rh negative mother; (3) an Rh positive baby without clinical signs, if the maternal antibody titer has been shown to increase during pregnancy; (4) a prematurely born, Rh positive baby of a sensitized mother who has no clinical signs; (5) an Rh positive baby without clinical signs, if there is a history of an earlier pregnancy in which the baby was seriously affected by erythroblastosis.

The technics for the various methods of replacement transfusion vary, and the reader is referred to the articles of Allen, Diamond and Vaughn[1-3] for details of the procedures and a discussion of their relative merits. It should be emphasized that a blood bank service and the skill and experience of a trained team of pediatricians are required for the smooth performance of the replacement type of transfusion and that it is hazardous and difficult for the inexperienced operator.

In the opinion of the writer, the standard type of small transfusion,[4] repeated as often as required to maintain good red blood cell and hemoglobin levels, is preferable to the replacement type unless an experienced operator is available.

Anemia in the late newborn period and the earlier months of life may result from factors which deprive the infant of its full quota of blood from the placenta. Premature separation of the placenta, cesarean section and early clamping of the cord rob the infant of a significant amount of blood. By early clamping of the cord, as much as 120 cc. of blood may be prevented from entering the fetal circulation. Premature and small babies, who are destined to exhaust rapidly the iron stores obtained from maternal supply during rapid growth in body weight, will develop an anemia in the early weeks of life, and an iron deficiency anemia will persist for several months.

NUTRITIONAL ANEMIAS

The nutritional anemias of infancy are due primarily to an iron deficiency. The factors concerned with the iron deficiency are: (1) presence or absence of anemia in the mother; (2) the period of gestation; (3) the size of the infant at birth; (4) rapid growth in body weight; (5) the dietary supply of iron in the infant's diet; (6) absorption of iron from the gastrointestinal tract; (7) infection. Clinical studies have shown that anemia in the mother predisposes the infant to anemia and therefore the first step in prophylaxis begins with neonatal life. A pregnant woman who shows any degree of iron deficiency should receive 0.3 gm. of ferrous sulfate or more daily. The infant receives its stores of iron from the mother largely during the last six weeks of gestation so that premature birth results in a smaller fetal supply. Twins obviously are required to share the maternal supply of iron. Premature babies and twins, therefore, have a high iron requirement from their diet during their period of rapid growth in body weight and blood volume, and iron should be supplied to these infants at an early age, i.e., the first few weeks of life. A soluble form of ferrous iron should be given in orange juice or water between feedings.[5]

The dietary sources of iron for the infant are meat purees, vegetables and egg yolk. Feeding this diet within the first two months of life serves the multiple purpose of providing iron, proteins, minerals and conditioning the infant's taste for a variety of foods. The milk-fed baby

who refuses these accessory foods into the seventh, eighth or ninth month of life develops a true iron deficiency anemia which is microcytic and hypochromic and responds rapidly to medicinal iron with a peak rise in reticulocytes and rapidly rising hemoglobin and red count. This iron deficiency anemia, or "cow's milk" anemia, does not require B_{12}, folic acid, liver extract or other vitamin B fractions. In "goat's milk" anemia the iron deficiency is complicated by a deficiency of folic acid, and folic acid is required as well as iron for adequate management of the condition.

MEGALOBLASTIC ANEMIA

Megaloblastic anemia in infancy is a nutritional anemia which responds specifically to folic acid. It is one of the last entities to be separated from the ill defined syndrome of von Jaksch's anemia. It occurs between the fifth and eleventh month, as a rule, and is due either to a deficiency of folic acid in the diet or to an inability of the infant to absorb and utilize this vitamin. Human milk and goat's milk contain less folic acid than cow's milk and infants fed exclusively on human or goat's milk are more apt to develop this syndrome, particularly if there is also a deficiency of ascorbic acid in the diet. The response to oral administration of folic acid is prompt. Ascorbic acid may also be required if a deficiency exists.[6] Vitamin B_{12} is less effective than folic acid. The best regimen for control of this anemia is obtained by the oral administration of folic acid 15 mg. daily and ascorbic acid 100 mg. daily. In severely ill babies, liver extract—2 cc.—may be used intramuscularly as well.

The response to therapy is indicated by an increase in blood reticulocytes followed by a rise in the red count and reversal of the megaloblastic marrow to the normal erythroblastic pattern. Once the hematologic response has been obtained and the dietary sources of folic acid are continued, the anemia does not recur as a rule. In a few isolated cases relapses have occurred, but it is thought that in these particular children some abnormality of the intrinsic factor of Castle is at fault.

ANEMIA OF INFECTION

In older children, anemia is more commonly due to infection than to a nutritional deficiency per se. The anemia of infection is a hypochromic anemia and the mechanism of the defective iron metabolism is still not clearly understood. It is known that during chronic infection the absorption of iron from the gastrointestinal tract is impaired, that the plasma iron falls, that parenterally administered iron is rapidly removed from the blood serum and that the concentration of metal-binding protein in the serum is decreased. Poor appetite during infection may reduce the intake of iron-containing food, and hypochlorhydria may impair the absorption of iron from the gastrointestinal tract, but since parenterally administered iron fails to cure the anemia, it seems apparent that the reduction in the amount of iron absorbed is not the essential factor in the hypoferremia which exists. It has been shown that some of the iron is bound to the tissues in inflammatory conditions and that it is not available for hemoglobin synthesis.

It is a common clinical experience that, in the presence of infection, anemias respond poorly to both orally and parenterally administered iron and transfusions may be required until the infection is controlled, if the anemia is severe. A word of caution is perhaps indicated against the continued use of intravenous iron medication during infection. Iron administered parenterally is excreted only in small amounts. If it cannot be utilized for synthesis of hemoglobin, the repeated use of parenteral iron medication may lead to hemosiderosis.

The anemias which develop in the chronic intestinal disorders such as ulcerative colitis, celiac disease and fibrocystic disease of the pancreas are usually iron deficiency anemias, although a multiple deficiency state may exist as well from the poor utilization of folic acid, ascorbic acid and protein. Iron administered orally may not be tolerated without increasing the tendency to diarrhea, and the judicious use of an intravenous preparation may be indicated.

Anemia due to blood loss in children is rarely difficult to recognize as it is usually the result of trauma and the bleeding is external. But it is well to remember that the only sign of a bleeding Meckel's diverticulum may be a gross

melena. Rapid blood loss may require a transfusion for the prevention of shock which often develops from a degree of anemia which would be tolerated well if it had developed slowly.

HEMOLYTIC ANEMIAS

Acquired hemolytic anemias of the acute or chronic type may develop at any time during childhood. The cause may be obscure or it may be traced to a bacterial toxin, a virus infection, or a vegetable or chemical toxin. Some of the agents known to produce the acute hemolytic anemias are: streptococci; the virus of infectious mononucleosis, of epidemic hepatitis and of pneumonia; arsenic; lead; sulfonamide, and the favus beans.

In the hemolytic anemias which result from infection, it is thought that the hemolytic process is due to immunologic factors; auto-agglutinins may be detected in the serum and it has been postulated that these are formed primarily in the spleen. However, since removal of the spleen does not regularly control the hemolytic process, it is apparent that the production of the hemolytic antibodies is not dependent solely upon the spleen. It has been shown recently that the administration of ACTH reduces the rate of hemolysis, but the mechanism of its inhibiting effect on the hemolytic process is not clear. In the acute forms of hemolytic anemias, treatment consists of transfusion with compatible blood and, in a large majority of cases, the response to supportive transfusion is prompt. In the more chronic cases, repeated transfusions, ACTH and even splenectomy may be indicated.

The three constitutional hemolytic anemias—Mediterranean anemia, sickle cell anemia and congenital hemolytic anemia—are all chronic anemias with a strong racial or familial hereditary factor.

Congenital hemolytic anemia, or spherocytic anemia, is the only form which responds satisfactorily to treatment. The diagnosis is established by the familial tendency to anemia and splenomegaly in one or more members of the family, and the demonstration of anemia, jaundice, spherocytosis and increased fragility of the patient's red blood cells to hypotonic saline. Splenectomy controls the anemia, as a rule, although spherocytosis persists throughout life. Although children with mild forms of this disease may tolerate a mild degree of anemia through childhood without splenectomy, they are subject to hemolytic crises, and splenectomy is advisable in early childhood whenever a patient shows a significant degree of anemia.

Mediterranean anemia, or thalassemia, has three clinical forms—major, minor and minima. The minor form characteristically shows a chronic microcytic and hypochromic mild anemia which is usually not severe enough to affect the general health unfavorably or to produce severe signs of anemia. Hemolytic crises are rare. Bone changes do not occur and no treatment is necessary other than general hygienic care. Thalassemia minima produces no clinical manifestations of the disease, but the defect in the erythrocytes can be demonstrated by an increased resistance to hypotonic saline; this form of the disease is known as the carrier state. Thalassemia major is a grave and progressive disease characterized by anemia, splenomegaly and progressive bone changes of the osteoporotic type. No adequate control of the disease is known other than supportive transfusions of whole blood or packed red cells. Few children survive beyond the early years of childhood and death usually results from the effects of a severe anemia and hemosiderosis.

Sickle cell anemia occurs in about 1 per cent of the Negro population, although 7 to 10 per cent of Negroes show the sickling trait. The child with sickle cell anemia is subject to repeated crises which are often characterized by severe abdominal pain—frequently misdiagnosed as an acute abdomen. The cause of the abdominal pain is usually splenic infarct. Demonstration of the sickling trait in the presence of anemia in a Negro child with acute abdominal pain will establish the diagnosis. Sickle cell anemia is a chronic disease which continues into adult life. Supportive transfusions are indicated to protect the growing child against the effects of anemia and cardiac complications. It is unwise to attempt to maintain normal levels of hemoglobin and red blood counts, because of the danger of hemosiderosis. A level of 9 to 10 gm. of hemoglobin will permit a reasonable degree of activity and good health.

APLASTIC AND HYPOPLASTIC ANEMIAS

Lastly, there is a group of anemias in children which are congenital in origin, and which are due to an aplasia or hypoplasia of the blood-forming organs, primarily the bone marrow. The "pure red cell" anemia is a clearcut entity which is recognizable in the early weeks of life and is characterized by a chronic severe anemia and a paucity of normal erythroblastic cells in the marrow. The production of other blood cells is normal and there is no hemorrhagic tendency. The condition is incompatible with life and the patient is dependent upon repeated blood transfusions. Transfusions are tolerated well and, with dogged persistence in controlling the anemia, a spontaneous recovery may be expected, even after a period of years.

The aplastic and hypoplastic anemias may be idiopathic or secondary to noxious agents or to primary blood dyscrasia such as leukemias or to malignancies which invade the bone marrow. The idiopathic types are chronic and often associated with other congenital defects, malformation of the skeleton or dwarfism. Treatment is unsatisfactory and dependent upon control of the hemorrhagic symptoms and anemia with transfusions. The secondary types, particularly those due to noxious agents, require intensive therapy with transfusions until a spontaneous regeneration of the marrow takes place. ACTH has been useful in some of these cases and appears to allow a more rapid regeneration of the marrow, although the mechanism of its action is not clear.

In summary it can be said that the management of anemia in children requires an appreciation of the factors concerned with blood formation and destruction in early infancy, the nutritional requirements of the growing child, and the effects of illness, noxious agents and constitutional defects upon the organs of hematopoiesis. The therapeutic armamentarium is limited but specific in its known effects, and the judicious use of the blood bank is a life-saving measure which tides many a child over a critical period. There are definite indications for the use of iron, folic acid, vitamin B_{12} and liver in the treatment of anemias in children. When blood transfusions are indicated, ascertaining the specific blood type of the patient to avoid sensitization by the use of an incompatible blood, and thereby predisposing the patient to a transfusion reaction at a later time, is one of the many obligations of the physician.

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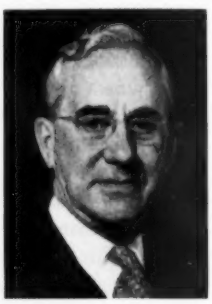
PORTRAIT OF FRANCIS G. BLAKE PRESENTED TO YALE

A portrait of Dr. Francis G. Blake, Sterling Professor of Medicine and former Dean of the Yale Medical School, was formally presented to Yale University as a gift of over 400 former colleagues, students, friends and members of the Medical School staff. It was painted by Raymond P. R. Neilson, a distinguished portrait painter.



DR. BLAKE

Dr. Blake just completed his thirtieth year of service at Yale and is retiring to go to Washington where he will serve with the medical research and development program for the U.S. armed forces.

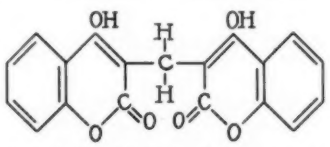
Dr. Blake joined the Yale Medical School faculty as a Professor of Medicine in 1921. In 1940 he became Dean of the School of Medicine, a position he held for seven years. He has held many positions of national importance in the field of medicine and in 1945, received the Charles V. Chapin Memorial Award. Dr. Blake also is a member of the Medical Advisory Board for *Postgraduate Medicine*.

Scientific Exhibit

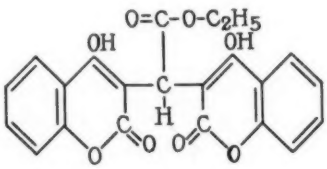
The Management of Oral Anticoagulant Therapy

SHEPARD SHAPIRO*

NEW YORK UNIVERSITY COLLEGE OF MEDICINE, NEW YORK CITY

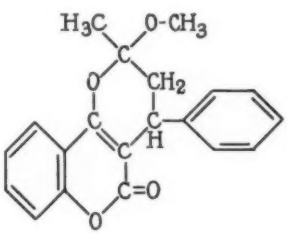


3, 3′-methylenebis (4-hydroxycoumarin)
(DICUMAROL)



3, 3′-carboxymethylenebis
(4-hydroxycoumarin) ethyl ester

(TROMEXAN)



2-methyl-2-methoxy-4-phenyl-
5-oxodihydropyrano-(3, 2-c) (1)
benzopyran (4-hydroxycoumarin)
(METHOPYRANORIN) COMPOUND No. 63

*Assistant Professor of Clinical Medicine, New York University College of Medicine, New York, New York.

THE AVAILABLE DRUGS... how they compare

	DICUMAROL	TROMEXAN	METHO-PYRANORIN *(Wisconsin No. 63)*	PHENYLIN-DANEDIONE
FORM	Tablets	Tablets	Tablets	Tablets
AVERAGE ABSORPTION TIME *(Days)*	1/4 — 1	1/6 — 1/4	1/4 — 2 (?)	1 — 4
AVERAGE DISPOSITION TIME***	25% per day	25% per hour	?	8 days
SIDE EFFECTS	None	None	None	Renal irritation?
COMPARABLE DOSE	300 mg.	900 mg.	150 mg.	900 mg.
COMPARABLE DAILY MAINTENANCE DOSE *(Method No. 1)*	200 mg.	600 — 900 mg.	50 — 100 mg.	400 — 600 mg.
AVERAGE FREQUENCY INTERMITTENT MAINTENANCE DOSE *(Method No. 2)*	5 — 7 days	Daily	7 — 10 days	Daily
COST PER 300 MG. DOSE*	$ .09	$ .20	**	**
COST PER DAY AVERAGE* DAILY MAINTENANCE DOSE	$ .06	$ .39	**	**
METHOD OF CONTROL	Prothrombin Estimation	Prothrombin Estimation	Prothrombin Estimation	Prothrombin Estimation
AVERAGE FREQUENCY LABORATORY TESTS FOR MAINTENANCE CONTROL	48 hours	12 — 24 hours	48 — 72 hours	24 hours

**At cost to pharmacist—Prescription mark-up not estimated. Dicumarol—Prices for 50 mg. tablets in 1000 package. Tromexan—Prices for 300 mg. tablets in 250 package. **Not available commercially (as of May 1951).*

***All references to the physiologic disposition of dicumarol and tromexan are based upon cooperative study with the New York University Research Division, Goldwater Memorial Hospital, New York City.

CALCULATION OF THE INITIAL DOSE OF DICUMAROL... 2 typical examples

FACTORS TO CONSIDER	EXAMPLE NO. 1	EXAMPLE NO. 2
WEIGHT OF PATIENT[1]	130 lbs.	150 lbs.
AGE OF PATIENT[2]	65 yrs.	40 yrs.
NUTRITIONAL STATE[3]	Poor	Good
ANEMIA[4]	Slight	None
LIVER FUNCTION[5]	Normal	Normal
INITIAL PROTHROMBIN TIME[6]	17 secs.	14 secs.
URGENCY[7]	Great	Great
HISTORY[8]	No previous accident	Previous accident at age 37
	For Daily Maintenance Method Initial Dose 300 mg. For Intermittent Maintenance Method 8 mg./kg. — 500 mg.	For Daily Maintenance Method Initial Dose 300 mg. For Intermittent Maintenance Method 10 mg./kg. — 700 mg.

1. In general, the initial dose can be calculated on the basis of

Dicumarol — 8 to 10 mg./kg.
Tromexan — 20 mg./kg.

Range is influenced by factors 2 to 8.

2. Patients in advanced age groups are often more sensitive and smaller doses are justified at the outset.

3. Patients in poor nutritional state are frequently more sensitive and yield marked responses to average doses.

4. Anemic patients are hypersensitive and may need less than average doses.

5. Liver function, if subnormal, may delay restoration of prothrombin time toward normal. Hence, smaller, less frequent doses are needed for maintenance therapy.

6. If initial prothrombin time is low, larger doses may be needed to obtain therapeutic response. Conversely, prolonged initial time indicates smaller doses.

7. If urgency is great and active thrombosis is present, one of the heparin-like drugs should be given intravenously and continued for 24 to 36 hours together with appropriate doses of oral anticoagulant until prothrombin estimation indicates therapeutic effectiveness of the dicumarol-like agent.

8. Previous history of thromboembolic accidents demands treatment on an "urgent" basis and indicates that prolonged anticoagulant therapy will be required.

CHOICE OF MAINTENANCE METHOD OF DICUMAROL ADMINISTRATION

	1 DAILY MAINTENANCE DOSE	2 INTERMITTENT MAINTENANCE DOSE
OBSERVATION PERIOD	The observation period, regardless of the maintenance method ultimately selected, must be long enough to determine the individual patient's pattern of response to the dose of dicumarol administered. Does the patient utilize and dispose of the drug quickly, at an average rate, or slowly? Does the patient require large successive doses, average doses or small? These questions can be answered within a few days after therapy is instituted by following daily estimations of prothrombin time and plotting a curve of the results.	
CALCULATION OF MAINTENANCE DOSE	Initial dose usually 300 mg., second dose on succeeding day usually 200 mg. Thereafter, dosage based upon prothrombin time, usually according to this scale: Time 30 seconds or less—Dose 100-200 mg. Time 30-35 seconds—Dose 50-100 mg. Time 35-40 seconds—Dose 50 mg. or less. Time 40 seconds or more—Dose is withheld.	One-half initial dose administered when prothrombin time is "falling," that is after peak response to preceding dose has been passed. Similar doses administered after successive peak responses noted.
USUAL FREQUENCY OF DOSE	Daily	5 — 7 days
FREQUENCY OF PROTHROMBIN ESTIMATION	Daily	Three times weekly
ADVANTAGES	(a) Believed that tendency to overdosage is reduced to minimum. (b) Easy to administer. (c) Develops routine or daily habit in patient. (d) Physician constantly aware of patient's prothrombin time.	(a) Cumulation is avoided. (b) The clinician is always able to determine which dose in terms of time is producing the response. (c) The number of prothrombin estimations is minimized. (d) Infrequent dosages.
DISADVANTAGES	(a) In the patient who transforms the drug abnormally slowly, cumulation is apt to occur. (b) It is not known at any one time to which dose of the drug the effect is due.	(a) Requires more knowledge of individual patient's responsiveness.

Either maintenance method may be used with perfect safety provided the clinician is able to follow the patient's response and the prothrombin estimations are reliable.

AN ILLUSTRATION OF THE TWO MAINTENANCE METHODS

IN THIS HISTORY: A patient was observed for 47 days. An initial dose of 600 mg. dicumarol was followed with 2 doses of 400 mg. each at 10 day intervals. On the twenty-ninth day, daily doses of 50 mg. were administered for five consecutive days, followed by 3 daily doses of 100 mg. each. Determination of plasma-dicumarol levels and estimation of prothrombin time were made frequently.

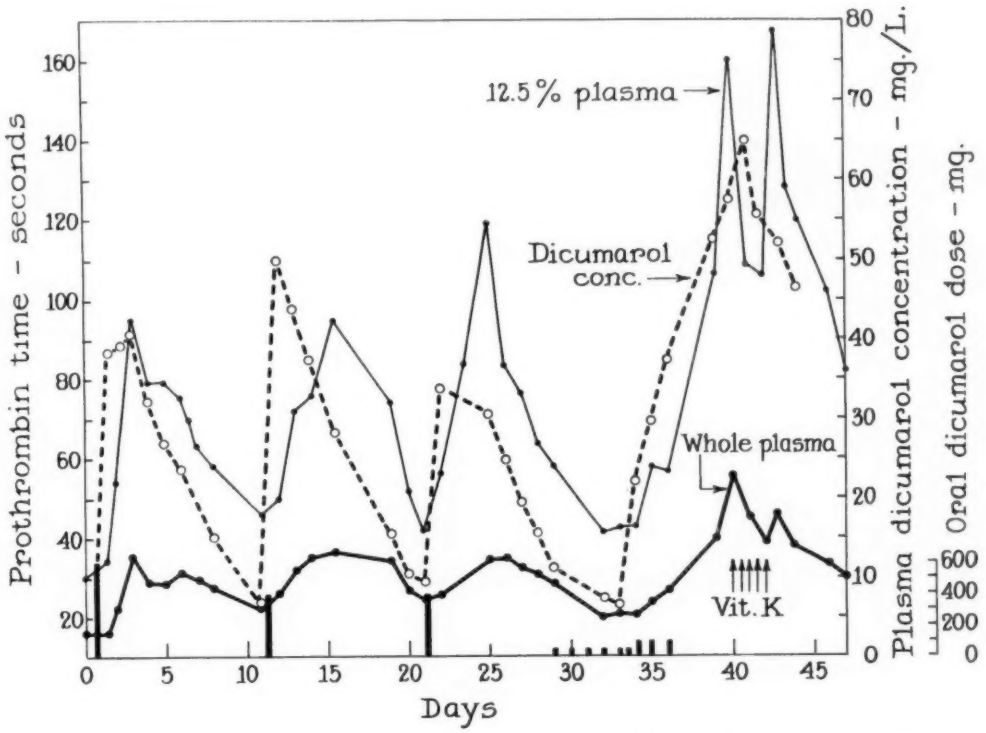


Illustration from: SHAPIRO, SHEPARD and WEINER, MURRAY: An evaluation of methods of dicumarol administration. Am. Heart J. 41:749-754 (May) 1951.

Both prothrombin estimation and plasma concentration indicate a smooth, predictable response in this patient to large, intermittent doses of dicumarol. Daily small maintenance doses may be relatively ineffective as shown by the response to five consecutive 50 mg. doses. On the other hand, slow transformation of the drug in this patient results in cumulation after about 10 days.

A PROBLEM PATIENT

THE PATIENT IS MALE	
WEIGHT	200 lbs.
AGE	75
NUTRITIONAL STATE	Fair
ANEMIA	Moderate
LIVER FUNCTION	Subnormal
INITIAL PROTHROMBIN TIME	Slightly increased
URGENCY	Great
HISTORY	Previous thrombosis at age 72

What dosages of heparin and dicumarol would you use?

ANSWER:

Because of the urgency involved an initial heparin dose of 75 mg. intravenously every six hours will be used and continued until a therapeutic response to dicumarol is obtained.

Dicumarol dose — 400 mg. (This is about half the dose for a younger patient with normal liver function.) To be followed by 200 mg. as soon as peak response is passed.

SAFETY IN MANAGING THE PATIENT AND THE THERAPY

1. In general, a dose which is clearly sufficient to reduce the danger of thrombosis is preferable to the risk of under-dosing. The number of deaths from hemorrhage caused by anticoagulant drugs is insignificant compared to fatalities from thromboembolic accidents.

2. In closely supervised patients, evidence of bleeding can be detected early and this condition may be rapidly corrected by administration of vitamin K.

3. The most practical index of therapeutic effectiveness of an oral anticoagulant is prothrombin estimation reported in terms of seconds. A level of two or two and one-half times the normal whole plasma prothrombin time usually indicates therapeutic effect.

4. Until recently, clinicians had sound reason to suspect the validity of laboratory tests reported to them. With the present availability of easily prepared, highly standardized thromboplastins, any competent clinical laboratory can obtain reliable results. All estimations of prothrombin time referred to in the studies indicated here were accomplished with SIMPLASTIN®* as the thromboplastin agent.

5. With careful inquiry into the patient's history and evaluation of the patient's probable capacity to absorb and utilize a dose of oral anticoagulant, combined with frequent observation during the first few days of treatment, a high degree of safety is readily attained by judging subsequent doses on the basis of the initial response pattern.

*Chilcott Laboratories, Division of The Maltine Company.

POSTGRADUATE
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EDITORIALS

JANUARY 1952

We regret
to announce the sudden and untimely death of the
Publisher of Postgraduate Medicine
MR. JACOB G. COHEN, Minneapolis
Mr. Cohen was a distinguished citizen of his community
and contributed greatly to its development
and welfare.

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SEPTEMBER 27, 1889 — DECEMBER 2, 1951

SPEAK UP, DOCTOR!

It has been said that the average person, in his daily oral communicating, uses 22,000 words. More specifically, it has been estimated that doctors use 598 spoken words for each written word. Whether or not these estimates are accurate, there seems to be little doubt that the routine work of the world is carried on by means of the spoken word. A minimum of introspection and observation leads us so unerringly to this conclusion as to obviate more precise measurement. That this is clearly recognized is attested to by the results of a survey cited by A. T. Weaver, Chairman of the Department of Speech at the University of Wisconsin.

> A 1950 survey of 140 industries, 20 large department stores, and 32 agencies of the federal government, employing a total of more than three million persons, showed that 90 per cent of these organizations were operating in-service training programs teaching conference participation, leadership and *public speaking*.

It has been characteristic of democratic societies, wherever they have appeared, that conclusions are reached, decisions made, and actions determined on the basis of an exchange of information, knowledge and experience among the members of the society. This has been so clearly recognized in our own society that we have taken great pains on a number of occasions to provide for and protect the right of free speech. We are inclined to ignore the fact that attending the rights with which we are blessed is the obligation to exercise those rights intelligently and effectively. Only by recognizing this obligation can our rights be maintained and preserved. To fulfill the obligation with which we are confronted we must prepare ourselves to share with others the results of our experience and the extent and nature of our knowledge. This involves, among other things, the necessity for acquiring or improving the ability to say things clearly, simply, and effectively.

The doctor may have one or several objectives in learning to speak well in public. Professional success may often depend upon the use of good speech in sharing knowledge and experience with colleagues. Effective speech may be of considerable value to the doctor in making a contribution, as a citizen, to the community and society of which he is a part. There are few occupations or professions where the training in thinking and doing is so extensive, intensive, and of such high quality as in medicine. The medical man's long period of training and experience in the scientific method should make extremely valuable his contributions to the public of which he becomes a part. But he must develop a reasonable skill and facility in applying the scientific method outside his own profession.

The doctor may find it helpful to use his speaking skill in furthering the cause of preventive medicine and public health. In recent years we have come to recognize as never before that the members of the medical profession are faced with the necessity of informing laymen of the nature, extent and quality of the service rendered by the profession. There is reason to believe that, while portions of this task may be left to outsiders, the job can be done most effectively by the individual members of the profession. If this job is to be done, every doctor must bear his share of the burden. You must speak up, doctor!

More and more doctors are recognizing the necessity for being able to speak well. Medical educators are beginning to require or recommend that premedical education include training in public speaking. The present course of study laid out for premedical students at the University of Minnesota includes a course in public speaking. For those already in the field whose training did not include adequate instruction in public speaking, it is not too late.

It is true that instruction in speaking is not adaptable to study by correspondence. One must learn by doing, and this calls for a group situation. Excellent textbooks are readily available and, in most communities, it is not too difficult to find a qualified and competent instructor. In many instances it should be possible to arrange for courses

through college or university extension divisions. A course in public speaking might well be sponsored by local and county medical societies. Acquisition of the desired skills will require time and effort, but the results are guaranteed to be worth while.

Frank Knox, former Secretary of the Navy, has said:

> Learning to speak is a valuable asset in the life of any man. It encourages self-confidence, develops character. Individual expression is the most cherished of democratic gifts. To be able to rise before an audience and speak extemporaneously sometimes tests the depths of what we call moral courage. To be able to do it successfully brings satisfaction and strength to face the problems of tomorrow. Through speech has come the power of the ages.

MASON A. HICKS
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RADIUM TOXICITY

During 1931 a number of mental patients in the Elgin (Illinois) State Hospital were given injections of radium chloride intravenously. About the same time patients in the Chicago area were being given radium water for arthritis by a few physicians and records are available indicating how much radium these patients received.

Now a group of workers in the Argonne National Laboratory, known as the Radium Toxicity Group, have completed a study* of 24 patients, 14 of whom received their radium chloride intravenously at the Elgin State Hospital and the remaining 10 in the Chicago area. At the time when the radium was administered, estimates indicated about 4.3 per cent of the radium remaining in the body after six months and 1.9 per cent after 12 months. Recent studies show that the amount of retained radium after 20 years was 0.8 per cent.

The new studies included complete roentgenographic examination of the skeleton on 19 of the 24 patients. Changes compatible with the diagnosis of aseptic necrosis were found in 7 patients, a partial loss of the mandible in 2 cases and a nonunion of the mandible in one. Fifteen of the 19 cases had changes that are described as "areas of decreased density, mottling or streaking."

The evidence is clear that radium plus various other unknown factors in the body may combine to produce degeneration of bone. Similar studies are now being made by an eastern group, headed by Dr. Joseph Aub, on 28 people who had radium more than 20 years ago.

MORRIS FISHBEIN

*A Progress Report of Clinical Studies on 24 Patients, by the Radium Toxicity Group, Division of Biologic and Medical Research, Argonne National Laboratory, July 1951. Report compiled and written by William B. Looney.

REHABILITATION IN INDUSTRIAL INJURIES

To the average workman, the payment of disability compensation affords little satisfaction. The loss of independence resulting from a serious injury, followed by a lengthy period of disability, often presents a severe economic and psychologic crisis for the workman and for his family. The longer an injured man is out of work the greater the possibility of his developing an anxiety state about the loss of his job. His recovery lags and consequently he becomes more depressed until finally he loses confidence in himself, in his doctor and in his employer. To regain confidence and efficiency a man must perform his former job or any other job compatible with his physical ability.

Rehabilitation is that phase of medical care which aims to bring about the full recovery of the patient's physical and mental functions which have been impaired by injury and to help him regain his capacity for earning his own living. If the patient cannot be returned to his former occupation, every effort must be made to prepare him for a new job which is compatible with his physical limitations. It is important to remember that rehabilitation includes psychologic as well as physical restoration.

Injuries most frequently encountered in industry are strains, sprains, amputations, fibrositis, myositis, traumatic injuries, fractures, dislocations and lacerations. During a period of two fiscal years, from October 1,

1948 to September 30, 1950, the Divison of Workmen's Compensation of the state of Alabama reported 1,239,185 man-days of lost working time. During this period the permanent partial injuries constituted 9 per cent of all nonfatal injury claims that were settled within one fiscal year. Of the total of these permanent partial disabilities, over 60 per cent consisted of finger injuries; the next largest group—over 10 per cent—involved toe and foot injuries, while hand injuries represented over 9 per cent of the total.[1] The loss in man-days of working time appears to be appallingly large in relation to the fact that the majority of these injuries involved only some of the digital extremities.

There is increased awareness on the part of industry of the possibilities inherent in physical medicine and rehabilitation. About 10 years ago Merck & Co. established a physical medicine department in Rahway, New Jersey to restore the functioning and hence the earning capacities of company employes. By 1944, 1,220 cases had been seen and treated—representing a saving of thousands of dollars and a considerable reduction in lost workdays. The examining physician, together with a psychiatrist who specializes in physical medicine and rehabilitation, complete a special form for each case, designating the patient's exact limitations. On the basis of this information the patient is assigned work for which he has the physical capacity.[2]

In 1949 Dr. Otto Eisert reported his findings on a study of 128 invalids whose average age was 55 and who had spent from a few months to 10 years in hospitals. After being retrained, 116 of the 128 patients achieved from 50 to 100 per cent capacity for self care. The majority were able to return to their homes and to perform such tasks as assembling, counting and classifying stocks.

The economic value of rehabilitated workers represents an impressive financial gain, as shown by figures released by the Office of Vocational Rehabilitation of the Federal Security Agency in a report on 41,925 workers rehabilitated during one fiscal year. "Average monthly earnings before rehabilitation were $24; average monthly earnings after rehabilitation, $147; total earnings annually before rehabilitation, $12,074,400, and total earnings annually after rehabilitation, $73,855,700."[3]

Are the handicapped as efficient and reliable as other employes? The Bureau of Labor Statistics reports that they are excellent employment risks. A careful study of the performance of 11,000 impaired workers and 18,000 unimpaired workers, subjected to the same job incentives and exposed to the same job hazards, established an identical frequency rate of nondisabling injuries and the average rate of absenteeism for the two groups showed no significant difference. The impaired workers did produce at a slightly higher rate and encountered slightly fewer disabling work injuries than did the unimpaired workers at the same jobs.[4] It seems that the compensatory law of nature makes adjustments in the abilities and potentialities of handicapped men.

To preserve valuable manpower in industry and to reduce time lost due to injuries, rehabilitation workshops could be established within industrial plants. Here a physical therapy department, supervised by a specialist, would reduce medical and transportation costs and would save time. A team of medical and industrial specialists could organize guidance or retraining programs. It is possible to manufacture special attachments for drill presses, planers and sanding machines, for instance, to aid the functioning of injured extremities. In the case of more severely handicapped workers, re-education for a suitable job can help the injured person to regain his earning power and consequently his self-confidence.

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